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COSTEN'S SYNDROME: A HITHERTO UNRECOGNIZED CAUSE OF VAGUE HEAD PAIN.[1]

By JAMES C. R. BELL, Dip.D.S.,
Perth.

THE word "syndrome" comes from the Greek *σύνδρομοι*, meaning "a running together, a meeting". "Stedman's Medical Dictionary" defines "syndrome" as follows: "The aggregate of symptoms associated with any morbid process, and constituting together the picture of the disease. The term is employed especially, though not exclusively, in relation to the grouped symptoms of disease of the central nervous system." Costen's syndrome, named after James B. Costen, M.D., of St. Louis, United States of America, is certainly a condition having an "aggregate of symptoms", and since 1933, when Costen first directed the serious consideration of the medical profession to ear symptoms consequent upon temporo-mandibular joint abnormality, considerable literature relative to the syndrome has appeared in American dental journals.

Earlier writings expressed a consciousness of the symptoms related to temporo-mandibular joint movement, and in about the years from 1925 to 1930 Edward C. Kirke, D.D.S., of the University of Pennsylvania, inspired a more thorough investigation into the problem within the realm of dentistry. To David Goodfriend, D.D.S., the professions of medicine and dentistry should be grateful for his researches into the subject about the year 1932. Goodfriend's publications were most informative and had, so to speak, a sense of scientific tension about them, so ardently did he strive to discover the entire truth. Prentiss was another prominent investigator in the field about that time. In more recent years such men as Higley, Riesner, Armstrong, Bleiker, Block, and Harris (dentists) and Batson and Chor (medical practitioners) have added much to our knowledge of the subject.

My objective tonight is to give you an introduction to an exceedingly complex problem without claiming to impart anything new or original. Neither do I wish to imply that Costen's syndrome has been worked out to the stage of scientific finality. There is still much to be done. I am inclined to believe that as familiarity with the syndrome matures, medical practitioners will be able to diagnose the syndrome in a clinical sense; but to dental practitioners will be left the detailed technique of both diagnosis and treatment. And to the dentists let me say that, generally speaking, our present status in anatomy, in radiology and in prosthetics—the tripod upon which successful handling of these cases is based—is inadequate. The time has arrived when the line of demarcation between medicine and dentistry is losing its clarity: when the doctor confronts problems which place his patients before the oral diagnostician: when the oral diagnostician must extend both his academic and technical horizon to meet the situation.

Today, patients suffering from Costen's syndrome are consulting both medical and dental practitioners and receiving neither diagnosis nor treatment. The general medical practitioner is usually the first to be consulted, not the dentist. The somewhat disjointed account of the symptoms by the patient to the doctor does not "make sense" to the doctor. In a well-established case the symptoms are often so bizarre that physicians, surgeons, rhinologists, dermatologists, oculists and dentists are all in due course consulted. Innumerable opinions are expressed, odd portions of the anatomy are excised, lavaged, drugged and manipulated, but the result is completely negative. In not a few of the cases, when a diagnosis is eventually arrived at, the mental state of the patient is such that one cannot get the cooperation so necessary to successful treatment.

[1] Read at a combined meeting of the Western Australian Branches of the British Medical Association and the Australian Dental Association on April 17, 1946.

General Principles.

It is comparatively easy to explain the general principles involved in Costen's syndrome, but exceedingly difficult to discuss the details. In general, the symptoms arise because the mandibular condyle does not take up a normal position in the articular portion of the mandibular fossa (glenoid fossa) throughout the various excursions of the mandible, these latter movements being controlled by the position of the teeth.

The complexity of the temporo-mandibular joint may be gathered from a perusal of the literature, particularly with regard to the actual movement of the meniscus and condylar head in the functional joint. The dental profession has conducted endless research in an endeavour to devise a means of actually measuring the movement of the condyle in the opening, closing, protrusive, retrusive and lateral excursions of the mandible. This research gave birth to the anatomical articulator, an instrument used by the dentist in the construction of artificial dentures. It is held that by using this articulator the dentist is able so to place the cusps of the artificial teeth that their functional contact harmonizes with the movements of the condyle in such a way that the occlusion of the teeth is balanced and the artificial dentures therefore are more stable. There are two schools of thought with reference to anatomical articulators. I myself think that too much is claimed by those who use them. The instrument does not measure condylar movement accurately, and therefore cannot give really accurate functional balance in a series of joint relationships where the condyle will not conveniently accommodate the margin of error.

FIGURE I.

Outline of condyle superimposed on face, showing pivotal point. Wax trial bite blocks, used in the course of denture construction, are *in situ*. Reproduced from Schlosser's "Full Denture Prosthesis".

An important aspect of denture construction is the degree of opening or closure of the jaws with artificial dentures *in situ*. This is referred to as the vertical dimension. If the vertical dimension is decreased (that is, the bite closed, or if the mandible is allowed to approximate the maxillæ beyond normal limits), not only will the facial musculature soon reflect the closure, but the condyle in some cases will also be influenced, in that it will take up an abnormal position in the condylar fossa; this in turn will lead to Costen's syndrome.

The human dentition is certainly a superb example of biological engineering, the power and harmony of which we fail to appreciate. So prevalent are the diseases dental caries and *pyorrhœa alveolaris* that nowadays it is a phenomenal occurrence to observe a perfect set of teeth. The wonder is that with so much disturbance of the maxillo-mandibular relationship there are not more cases of Costen's syndrome.

The medical practitioner needs some easily applied diagnostic procedure which will enable him to relate the subjective pain complained of to the malfunction of the mandible. The symptoms enumerated later, once he knows how to piece the story together, will guide him towards

FIGURE II.

A: Artificial dentures are in place; the teeth are in occlusion. Extreme closure of the bite has caused a forward thrust of the mandible and sagging of the muscles of the mouth and nose. B: The same patient, with the vertical dimension brought back to normal by the construction of new dentures. Muscular tone has been restored and the mandible restored to normal position. After A. W. and J. M. Mann and J. D. Spies, *The Journal of the American Dental Association*, December, 1945.

a diagnosis. An examination of the mouth, facial characteristics *et cetera*, will generally more than hint at the loss of vertical dimension. Having gone thus far, if he presses over the condyle with moderately heavy pressure and instructs the patient to open the mouth widely and close it, he will generally find, in the genuine case of Costen's syndrome, one or both of the temporo-mandibular joints to be tender, objectively and subjectively. This simple clinical test, together with an awareness of the symptomatology and its cause, will in general allow of a tentative diagnosis and indicate the need for dental examination.

It has been my experience that the average patient suffering from Costen's syndrome experiences great difficulty in intelligently explaining the subjective symptoms.

The verbal account is disjointed, vague and variable, and it is not until the diagnostician knows how to piece the story together that a logical pattern emerges. Therein lies the ever-present danger of diagnosing only the malady one is looking for.

When a patient has suffered from the syndrome for many years, with increasing severity, superimposed upon the somatic factors may be psychological factors which at times most effectively cloud the issue. Often patients with genuine grounds for complaint are told that they suffer from "nerves". They go on year after year, eventually to become introspective. They then think in terms of cerebral tumour, malignant disease and suicide.

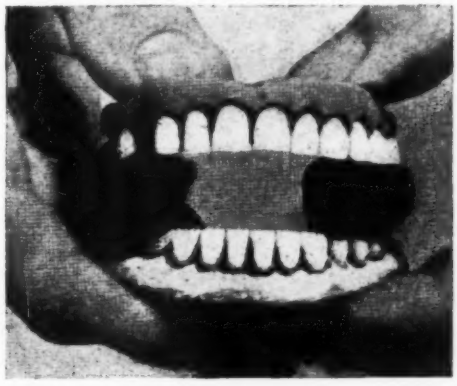

FIGURE III.

Dentures with wax bite blocks in place, showing distance between dentures in correct vertical dimension position. There is loss of the upper right first bicuspid and first molar denture teeth because of deterioration of the denture base material. These dentures have been in use for twenty-five years by the patient shown in Figure II. After A. W. and J. M. Mann and J. D. Spies, *The Journal of the American Dental Association*, December, 1945.

FIGURE IV.

Showing the effect of loss of vertical dimension (with closure) upon the facial musculature. Patients wearing artificial dentures are not the only persons who suffer from Costen's syndrome. In patients afflicted with the syndrome who have natural teeth only in the mouth, it will usually be found that loss of molar support is the explanation of the symptoms, and the symptoms may not enter the picture until five to seven years after the loss of the molar teeth.

Report of a Case.

A female patient, aged forty-five years, living in the country, was normal and well apart from persistent pain and buzzing in the ears and pain in the tongue. The severity of the symptoms increased slowly but surely until she journeyed to town, "in desperation", to use her own words. In fourteen days she had consulted eleven doctors and one dentist. A consultant physician talked vaguely of "nerves". A surgeon advised alcohol injections. A second consultant physician referred her to a dermatologist because of pain in the tongue. The dermatologist could see no cause for the pain. A general practitioner suggested taking vitamin *B*. An ear, nose and throat specialist suggested removal of the tonsils. An oculist found no abnormality in the eyes. So things went on, until the patient eventually consulted a general practitioner who suspected the possibility that dental factors might be the cause of the pain and referred her for dental examination. Within forty-eight hours of the insertion of dentures which established a normal maxillo-mandibular vertical dimension, the symptoms had subsided sufficiently to make it clear that she was suffering from Costen's syndrome. In three weeks the patient was entirely free from pain.

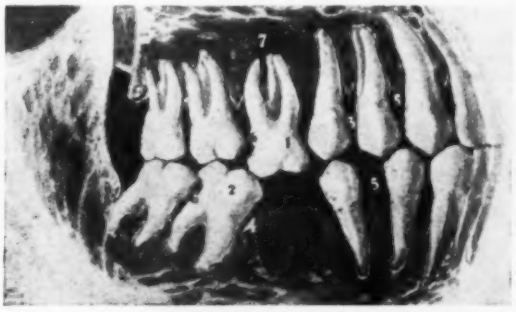

FIGURE V.

Showing how malocclusion may predispose towards premature loss of the molar teeth as a result of caries. Reproduced from *Dental Digest*.

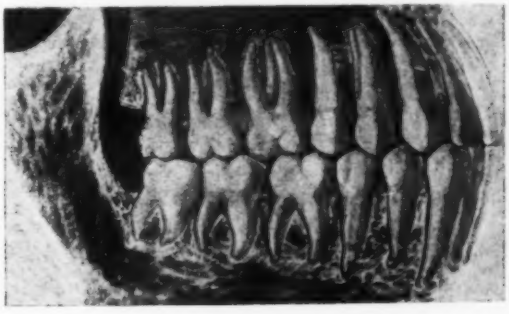

FIGURE VI.

Showing the complete dentition in perfect occlusion. Reproduced from *Dental Digest*.

Symptoms.

Not all patients present with all the symptoms, which are as follows:[3] (i) pain, dull in type, within and about the ears; (ii) tinnitus, usually "low buzz" in type, less often a snapping noise when chewing; (iii) a "stuffy" sensation in the ears, pronounced about meal times; (iv) mild catarrhal deafness, which is relieved by inflation of the Eustachian tubes; (v) dizzy spells, relieved by inflation of the Eustachian tubes; (vi) tenderness to palpation of the temporo-mandibular joints; (vii) typical sinus headaches after sinus or eye involvement has been corrected or found to be non-existent; (viii) traumatic, noisy, painful, limited or excessive movement of the temporo-mandibular articulation; (ix) neuralgia; (x) a burning or prickling sensation of the tongue, the throat and the side of the nose; accompanying this sensation slight herpes of the affected part may be present; (xi) a metallic taste;

(xii) dryness of the mouth, due to disturbed function of the salivary glands; (xiii) a feeling of fullness in the nasopharynx; Batson states: "We may have here the explanation of the symptoms of which so many of the older patients complain, the fullness of the pharynx and the accumulation of postnatal secretions"; (xiv) inability to swallow effectively.

The symptoms are so numerous and involve so many structures that a feeling of doubt enters the mind whether loss of vertical dimension can possibly cause so much trouble. Anatomical explanations must therefore be sought before the formidable list of symptoms can be accepted as related to the one cause. Many neurological details relative to the field under discussion, and formerly accepted as having been adequately explained by earlier anatomists, are still the subject of inquiry by many leading anatomists of today. The complex relationships between the facial, glosso-pharyngeal and trigeminal nerves have not yet been solved in their entirety.

A consideration of the symptoms reveals an anatomico-physiological grouping. Most of the symptoms come under one or other of these headings: (i) neurological, (ii) otological, (iii) muscular. With that classification in mind we shall review the anatomical detail.

FIGURE VII.

An X-ray film of the temporo-mandibular joint with a wire placed in the petro-tympanic fissure to represent the *chorda tympani* nerve. This illustration leaves little doubt that the mandibular condyle can, and does, exert pressure upon the *chorda tympani* nerve. The petro-tympanic fissure is an important feature.[10] It divides the mandibular fossa into two halves: (*a*) articular (anterior half, accommodating the condyle); (*b*) non-articular (posterior half, lodging portion of the parotid gland). Should the condyle be displaced posteriorly, the *chorda tympani* is encroached upon as it emerges from the petro-tympanic fissure—hence the various disturbances. Reproduced from *The Journal of the American Dental Association*, September, 1938, page 1390.

Neurological Symptoms.

The neurological symptoms are largely dependent upon the close relationship existing between the temporo-mandibular joint and two nerves, the auriculo-temporal nerve and the *chorda tympani*.

Auriculo-Temporal Nerve. The auriculo-temporal nerve[11] arises from the undivided trunk of the mandibular nerve by two roots which, before uniting, embrace the middle meningeal artery. The two roots communicate with (*a*) the otic ganglion (directly) and (*b*) the glosso-pharyngeal nerve (indirectly). The auriculo-temporal nerve then passes posteriorly just medially to the neck of the condyle, thence to the parotid gland, and superiorly to the temple

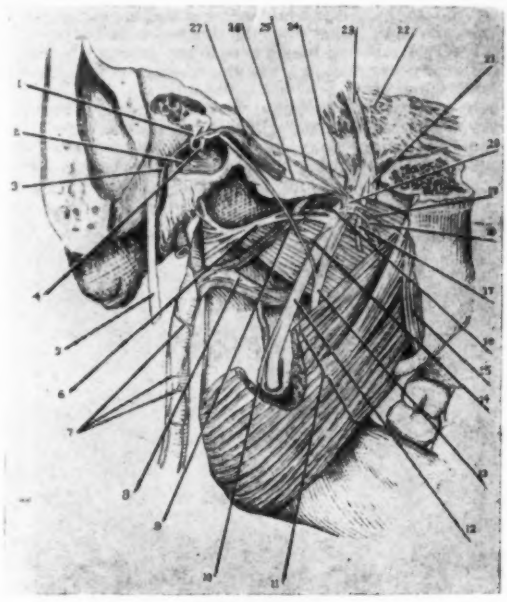

FIGURE VIII.

The otic ganglion or ganglion of Arnold, *ganglion oticum*, its roots and branches. Displayed on the left side of the head, and viewed from within. (Redrawn from Toldt.) 1: Long process of the incus. 2: Tympanic membrane. 3: *Chorda tympani* nerve. 4: Handle of the malleus. 5: Facial nerve. 6: Auriculo-temporal nerve. 7: External carotid plexus with its extensions, the internal maxillary plexus and the middle meningeal plexus. 8: Middle or great meningeal artery. 9: Sympathetic root of the otic ganglion. 10: Mylohyoid nerve. 11: Internal pterygoid muscle. 12: Inferior dental nerve. 13: Lingual nerve. 14: Communicating branch to the *chorda tympani* nerve. 15: Circumflexus or *tensor palati* muscle. 16: Communicating branch to the auriculo-temporal nerve. 17: External pterygoid nerve. 18: Internal pterygoid nerve. 19: Nerve to the *tensor palati* muscle. 20: Otic ganglion, or ganglion of Arnold. 21: Small, anterior or upper portion of the inferior maxillary nerve. 22: Large or sensory root of the fifth cranial, trifacial or trigeminal nerve. 23: Small or motor root of the fifth cranial, trifacial or trigeminal nerve. Reproduced from Smith's "Block Anesthesia".

over the zygoma with the superficial temporal artery. It is finally distributed as a cutaneous nerve of the temple and scalp and reaches almost to the vertex of the skull. When it is adjacent to the neck of the condyle, the nerve gives off a branch to the temporo-mandibular joint, so that irritation of the auriculo-temporal nerve is anatomically possible for the following two reasons: (i) fibres of the nerve actually enter the joint structure; (ii) unsupported movement of the condyle, mesially or posteriorly, causes trauma as the nerve passes close to the mesial side of the joint capsule.

In reviewing 165 cases of the syndrome, Costen[3] selected 94 patients as presenting the commonest type of clinical picture in the series. Of these he makes the following statement:

> They all complained of head pain. Almost all localized the pain as vertex, occipital, and about the ears, eighteen emphasizing supra-orbital distribution. If we disregard posterior sinus or eye disease, of which these were typical, but which were ruled out by absence of findings, anatomic reasons could be found within the pathologic mandibular joint.

Elsewhere Costen states that ". . . irritation of the auriculo-temporal nerve by impaction of the condyle is the chief etiologic factor in glossodynia, or burning tongue".

Chorda Tympani Nerve. The *chorda tympani* nerve,[12] a branch of the facial nerve, is even more closely related anatomically to the movements of the condyle than is the auriculo-temporal nerve. The *chorda tympani* arises

from the facial nerve in the facial canal of the temporal bone. It enters the tympanic cavity, passes over the *membrana tympani* and the handle of the malleus, and leaves the cavity through the mesial end of the petro-tympanic fissure to reach the infratemporal fossa. Under cover of the external pterygoid muscle the *chorda tympani* receives a branch from the otic ganglion and incorporates itself into the lingual branch of the mandibular nerve. The *chorda tympani* supplies a root to the submaxillary ganglion, and is finally distributed to the side and dorsum of the tongue in its anterior two thirds, giving the sense of taste thereto.

Sound waves pass down the external auditory meatus to impinge on the drum of the ear. The vibrations are thence transmitted by the malleus, incus and stapes across

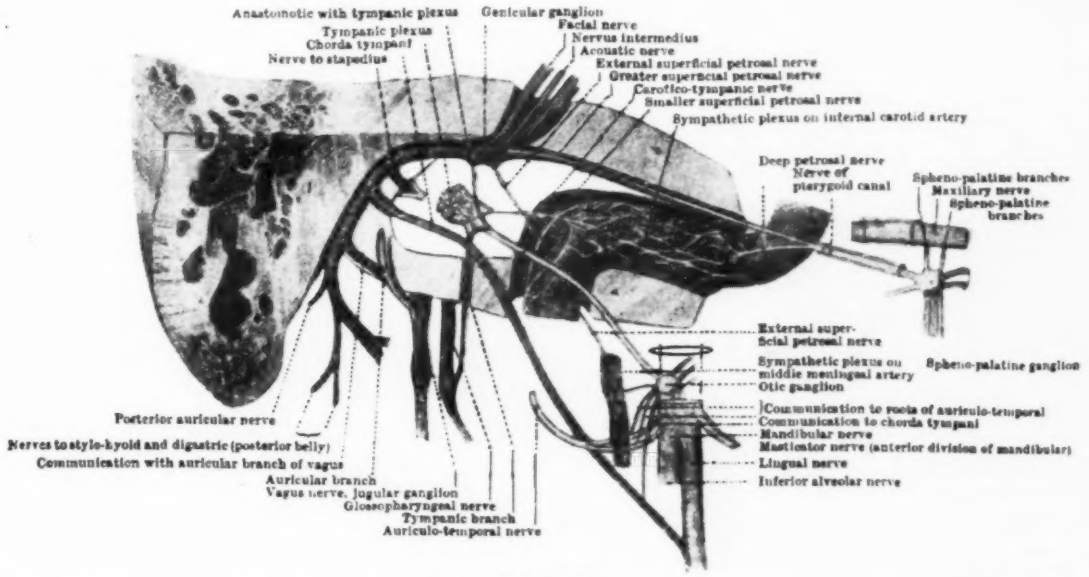

FIGURE IX.

The connexions of the facial nerve in the temporal bone. A diagrammatic illustration of the neurological complexity associated with Costen's syndrome. This diagram shows how the petrosal nerves serve to link up facial, glosso-pharyngeal and trigeminal nerves together with their ganglia and with the tympanic plexus.[6] When one studies this diagram, one appreciates the multiple symptoms seen in the syndrome and realizes that they are based on actual anatomy and not on surmise. (Reproduced from "Cunningham's Text Book of Anatomy".)

the cavity of the tympanum to the fluid which bathes the termination of the auditory nerve in the internal ear. The function of the tympanic apparatus is to transform the energy of the vibrations incident on the drum into a series of mechanical movements of the plunger of the stapes, by which the pressure within the internal ear is rapidly varied.[7]

From the point of view of the discussion this evening, on the labyrinthic or mesial wall of the tympanum is an important plexus, the tympanic plexus, formed by the carotico-tympanic nerves, the tympanic branch of the glosso-pharyngeal nerve, and a twig from the geniculate ganglion of the facial nerve. Remembering the relationship between the tympanic plexus and the facial, glosso-pharyngeal and trigeminal nerves, together with the actual passage of the *chorda tympani* nerve through the tympanic cavity, we are more able to appreciate the phenomenon of tinnitus and the aural symptoms in cases of Costen's syndrome and the frequently encountered case in which pain of dental origin is referred to the ear.

Muscular Symptoms.

In considering the muscular aspect of the syndrome, we must be prepared to discard the common conception of muscles as so many independent functional units, and look more at the functional interrelationship existing between various combinations of muscles.

George Christensen, D.D.S., of Queensland, in listing seven anatomical facts relative to alteration in the position of the mandible as a means of treating acute or chronic inflammation of the middle ear caused by repeated pressure differences on either side of the tympanic membrane in Royal Australian Air Force personnel, enumerates facts of extreme interest to either medical practitioner or dentist interested in the many facets of this problem of the loss of vertical dimension. Christensen's points are as follows:[9]

1. The *tensor veli palatini* muscle, which is attached directly to the medial lamina of the Eustachian tube and inserted in the palatal aponeurosis, is the muscle directly associated with the opening of the lumen of the tube.

2. The salpingo-pharyngeus, which is attached to the inferior aspect of the cartilaginous portion of the tube, is concerned with alteration of the angle between that portion of the tube and the bony portion, thus also helping to establish patency.

3. The opening of the mouth and depression of the mandible are accompanied by the contraction of the external pterygoid muscles, which pull the head of the condyle forward, the spheno-mandibular and stylo-mandibular ligaments then coming into play to fix the ramus, the mandible then rotating about an axis situated approximately in the region of the mandibular foramen. The stylo-mandibular ligament passes in close approximation to the junction of the cartilaginous and bony portions of the Eustachian tube and is capable of mechanically occluding the tube at this point.

4. Displacement of the condyle medially, as occurs in the right or left excursion of the mandible, can result in compression of the tube, the pressure being transmitted via the head of the external pterygoid and intervening soft structures.

5. In overclosure of the mandible the external pterygoid may become slack and bulge, resulting also in the mechanical occlusion of the tube.

6. The internal pterygoid is associated with the closure of the jaw, the extent of the closure being limited by the occlusion of the teeth. In cases of closed bite, the contraction distance of the internal pterygoid is decreased, its action hampered, and, as a result, it

may bulge medially and posteriorly along the superior head of the external pterygoid affecting the cartilaginous portion of the tube, resulting in compression.

7. In cases of closed bite all the muscles and tissues of the posterior wall of the pharynx are in a loose flaccid state, muscle tone being considerably diminished.

That Eustachian stenosis consequent upon malposition of the mandible can be relieved by reestablishing correct vertical dimension, and that the ventilation of the middle ear is thereby improved, are facts of clinical value. During the war number of grounded flying personnel were able to resume flying because the position of the condylar head consistent with normal vertical dimension and adequate ventilation of the middle ear was worked out and made possible by the wearing of a dental appliance. This development will extend into the realm of civil aviation, and it is not a fanciful flight of the imagination to visualize the air hostess of the future distributing some form of bite-block to passengers suffering from "ototic barotrauma".

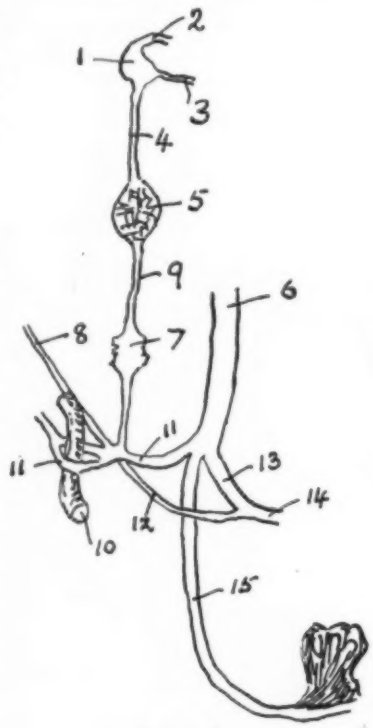

FIGURE X.

Course of reflex pain from the throat or a carious tooth to the ear. The reflex travels thus: From the tooth to the mandibular nerve, through the auriculo-temporal nerve to the otic ganglion; from the otic ganglion to the tympanic plexus through the small superficial petrosal nerve.[10] 1: Geniculate ganglion. 2: Facial nerve. 3: Great superficial petrosal nerve. 4: Small superficial petrosal nerve. 5: Tympanic plexus. 6: Third division of fifth nerve. 7: Otic ganglion. 8: *Chorda tympani* nerve. 9: Small superficial petrosal nerve. 10: Middle meningeal artery. 11: Auriculo-temporal nerve. 12: *Chorda tympani* nerve. 13, 14: Lingual nerve. 15: Mandibular division of the trifacial nerve. Reproduced from Barnhill's "Surgical Anatomy of the Head and Neck".

Oscar V. Batson, M.A., M.D., of Philadelphia, has developed the "kinetic muscular chain" conception of the act of swallowing and its effect upon the Eustachian tube.[10] Batson states that "if we consider muscles according to the teachings of such anatomists as Braus, they are not anatomic entities named by the whim of some dissector, but to be considered in groups as they actually function".

With this conception of such a group of muscles, we can appreciate how, when the entire group is made to function inharmoniously because of the anatomical facts associated with closed vertical dimension, the patient experiences fullness of the pharynx and accumulation of post-nasal secretion—symptoms which the patient finds almost impossible to describe in a way acceptable to the clinician not fully aware of the actuality of the circumstances.

From the diagrammatic illustration by Batson, let us pass to a more detailed illustration of the tubal and palatal muscles (Figure XII). This drawing gives an excellent idea of the attachment, insertion and function of the tubal and palatal muscles. It should be studied in conjunction with a good skull. The *tensor palati* and the salpinogopharyngeus are the two muscles mostly concerned with the opening and closing of the Eustachian tube, the tensor playing the major part.

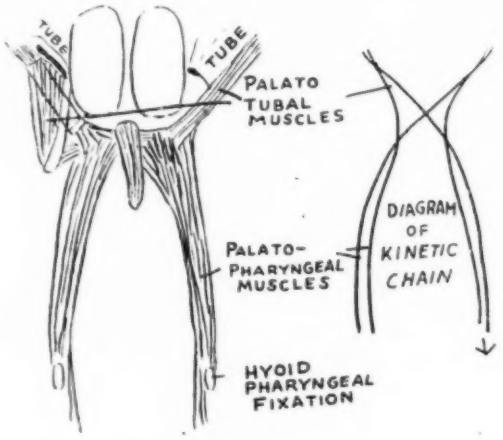

FIGURE XI.

Schematic representation of palato-salpingo-pharyngeal muscles as seen from behind. The diagram indicates the physiological continuity of these muscles and draws attention to the error of considering the muscle bundles as isolated anatomical entities. The flaccidity of this kinetic chain in a case of closed bite interferes with an effective contraction. Reproduced from *The Journal of the American Dental Association*, August, 1938, page 1191.

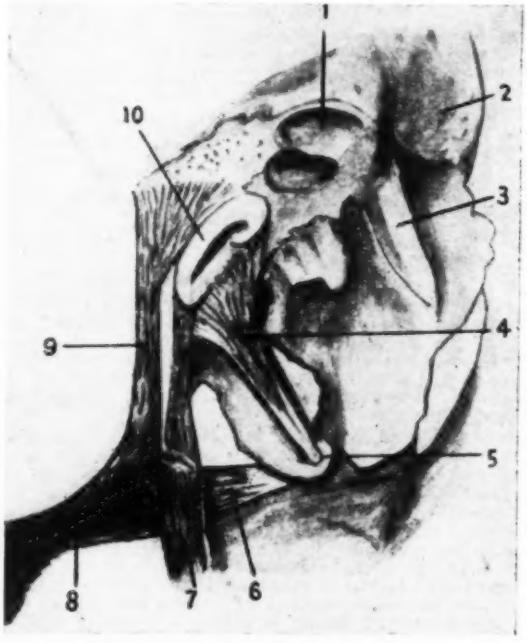

FIGURE XII.

View looking upward and backward, showing specimen in which the muscles of the auditory tube and soft palate have been dissected out. 1: Glenoid fossa. 2: Mastoid process. 3: Styloid process. 4: *Tensor palati* muscle. 5: Hamulus or pterygoid process. 6: Belly of *tensor palati* beyond the hamular process. 7. Salpingo-pharyngeus. 8: Interlacing of muscle fibres in palate. 9: *Levator palati* muscle. 10: Auditory tube cut across showing the attachment of muscles. Reproduced from Barnhill's "Surgical Anatomy of the Head and Neck".

Comment.

We thus conclude a *résumé* of the neurological, otological and muscular factors associated with the loss of vertical dimension, and perhaps at this stage you will not be so reluctant to acknowledge that the symptoms of Costen's syndrome, even though bizarre and numerous, are possible. Much has been written; much remains to be investigated. It is commonly assumed that we have gone a long way in anatomy; but there is not the equally facile assumption that we still have a great deal to learn, not so much from the structural as from the functional point of view. The interrelationships rendered so complex, and seemingly endless, in both harmony and disharmony are even today at times beyond our clinical sense, and we ascribe the quality of incoherence to statements made by those before us in the consulting room.

In conclusion, let me add a note of warning, that opening of the bite is not a responsibility to be accepted lightly. If the vertical dimension is increased when it should be left alone, or if it is increased beyond the amount required to accomplish anatomical and physiological rehabilitation of the joint, the patient suffers intense pain beyond the level of endurance and considerable damage can be done.[11] Psychologically and anatomically, the time factor should also be considered. What may appear to be a legitimate procedure now, may a few years later result in irreparable damage to alveolar ridges, muscle tone and condyle function.

The entire story has not been told. But the fact remains that the oral diagnostician can be of assistance to the medical profession, because in so many cases correct diagnosis and treatment have been effected by opening of the bite that the results speak for themselves, and the procedure has established itself as a definite entity in modern therapy. We can no longer tell these patients that they are suffering from "nerves" (to the consultant a word of comforting vacuity) and leave them to the mercies of traumatized temporo-mandibular joints. Both professions need men who will make a profound study of this problem, and such men should be appointed to general and dental hospitals, so that their knowledge and skill will be not only available but also applicable to patients requiring their services. The treatment of these patients can at times be handled by the general practitioner with his generalized technique; but as such patients present in greater numbers, because the syndrome is now a recognized clinical entity, it will be found that by and large their successful treatment will call for special knowledge and application altogether free of economic considerations, and influenced for the good by the cooperative endeavour more often seen in hospital practice than elsewhere. Practitioners, medical and dental, should be able to refer these patients to such an institution as a dental hospital, knowing that they will be handled by a man not only conversant with all the academic data, but also possessed of the radiological and prosthetic skill to see a patient through all the vicissitudes to a successful outcome, for not all patients can be treated by rule-of-thumb procedure. The general hospital will need such a man on its staff to assist the physician and surgeon to arive at a diagnosis and bring together the radiological and prosthetic factors so essential to successful treatment. As maxillo-facial surgery brings doctor and dentist together as a cooperative team, so will Costen's syndrome.

Conclusions.

In Costen's syndrome we have a hitherto unrecognized cause of vague head pain, which many patients have endeavoured to describe to us with but little success, as they have so often been informed that they are suffering from "nerves".

The symptomatology is so complex that the clinician needs to be aware of this clinical entity before he can interpret the apparently irrelevant statements made by the patient.

Treatment of Costen's syndrome by increasing the maxillo-mandibular vertical dimension is an established therapeutic procedure which calls for clinical discernment and judgement. It is not a rule-of-thumb procedure. In referring the patient to the dentist the doctor should not imply that it is simply a matter of having the dentures altered; otherwise the dentist may fail to receive the degree of continuity of cooperation that is so necessary before ultimate success can be achieved.

Increase in the vertical dimension in the course of denture construction is a responsibility not to be accepted lightly, as the procedure often involves both patient and dentist in various technical vicissitudes. If it is overindulged in, it may also bring about loss of valuable bone in the course of time.

Not all patients present with all the symptoms. In fact, an isolated symptom may appear and not be recognized as a manifestation of the syndrome. Response to treatment varies according to the degree of existent abnormality and nerve trauma. The average patient reports relief from pain within forty-eight hours of joint rehabilitation, followed by complete relief from all symptoms two or three weeks after treatment.

From the dental point of view the difficulty is to decide just what increase in vertical dimension the patient can accommodate, as distinct from the degree of opening theoretically indicated. Few patients can tolerate the change from the original condition to the theoretically normal in one step. The average patient obtains relief with less than the theoretically normal degree of opening; but occasionally the considered normal must be accomplished by periodical changing of the dentures—a not easily overcome economic factor at times.

The relationship between the facial, glosso-pharyngeal and trigeminal nerves has not yet been fully comprehended; therefore our knowledge of Costen's syndrome is not complete. Until such time as both the medical and dental professions become generally aware of Costen's syndrome, many patients will pay futile visits to our consulting rooms; they will be submitted to needless surgery; they will be obliged to contend with needless suffering.

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GENERALIZED LYMPHATIC CARCINOMATOSIS (CANCEROUS LYMPHANGITIS) OF THE LUNGS, WITH SPECIAL REFERENCE TO MILIARY CARCINOMATOSIS AND THE SYNDROME OF "GRANULIE FROIDE".

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IT has been known for some years that skiagrams showing disseminated miliary lesions in the lungs giving an appearance resembling that of miliary tuberculosis may occasionally be obtained on radiological examination of patients who exhibit no pyrexia and whose general condition appears to be fairly satisfactory. In such cases recovery is possible and the miliary lesions may disappear

entirely, although the course of the illness may be prolonged.

Such a condition is known among French physicians as "*granulie froide*", "*granulie apyrétique*" or "*granulie chronique*", and since it has been regarded as a type of tuberculosis it has also been called "apyrexial miliary tuberculosis" and "subacute or chronic miliary tuberculosis". However, a perusal of Burnand and Sayé's[1] classical paper on the subject in the light of recent work leaves one unconvinced regarding the role of tuberculous infection in all of the cases described, owing to the meagre record of the pathological and bacteriological data. But in view of the pathological evidence subsequently brought forward by Burnand[2] and by Hoyle and Vaizey,[3] the possibility of the existence of chronic miliary tuberculosis cannot be set aside.

Since the publication of the papers by Burnand and Sayé, at least one important condition capable of causing *granulie froide*, of apparently non-tuberculous origin, has been differentiated—namely, the Besnier-Boeck-Schaumann syndrome.

A general account of this syndrome, together with a report of cases illustrating the difficulties of establishing the diagnosis when the localization of the lesions is restricted to the lungs, has already been published in this journal.[3a] In view of the close resemblance between this disease and tuberculosis in respect of the clinical and pathological features, a diagnosis of chronic or apyrexial miliary tuberculosis should be regarded with scepticism. A further possibility to be borne in mind is that tuberculosis and sarcoids may coexist, as in cases described by Schaumann,[34] [35] and that tubercle bacilli may invade sarcoids causing secondary caseation and calcification, just as they may invade lymphogranulomatous tissue or new-growth of the lungs (Kikuth).[36] Some cases recorded as of chronic miliary tuberculosis, in which tubercle bacilli have been demonstrated, may have been due to sarcoids complicated by tuberculosis.

It is necessary to emphasize that the conception of *granulie froide* is based essentially upon the results of radiological examination; but from the presence of shadows indicating disseminated miliary lesions in the lungs, it is unjustifiable to draw conclusions regarding either the ætiology or the histological characters of the lesions.

Similar appearances may be met with in a number of conditions, including pneumonokoniosis, mycotic diseases of the lungs, lymphogranulomatosis, *et cetera*. The case here recorded illustrates another important, although uncommon, condition producing the radiological and clinical features of *granulie froide*—namely, miliary carcinomatosis of the lungs.

Report of a Case.

The patient, A.McL., was a woman, aged thirty-four years, who had been in her usual health until June, 1940, when she first came under medical care owing to an attack of "influenza", which was followed by a dry cough. Owing to the persistence of the cough she was referred to the tuberculosis clinic of the Royal Prince Alfred Hospital, but a radiograph of her chest taken five months after the onset of her illness revealed no recognizable abnormality. In January, 1941, with the occurrence of fresh "colds", she began to bring up some sputum, and about the same time she complained of a pain in the back over the lower ribs. She continued in this way until April, 1941, when all her symptoms became exacerbated. The cough became more severe and the sputum more abundant, and on one occasion she brought up about half a cupful of blood. She also experienced increasing weakness, loss of appetite and loss of weight (she had lost one and a half stone in weight since the beginning of the year), while on several occasions she had night sweats. On May 20, 1941, she was admitted to the wards of the Royal Prince Alfred Hospital under the care of Dr. R. S. Steel.

The patient had enjoyed good health all her life, and there was nothing in her history to suggest the presence of previous tuberculous disease. There was no history of tuberculosis in the family or amongst persons with whom she habitually came into contact. Her occupation was that of a pantry worker and her diet and home conditions were satisfactory.

Examination of the patient soon after her admission to hospital revealed her to be a rather thin, pale woman with a hacking cough. No obvious abnormality was detected in the shape or movements of the chest. There was some impairment of resonance at the base of the right lung, and broncho-vesicular breath sounds were heard in the inter-scapular region on the left side. Elsewhere the breath sounds were normal and there were no adventitious sounds. Some tenderness of the chest wall was encountered over the lower part of the thorax posteriorly on the right side.

X-ray examination of the chest, made on May 23, 1941, revealed the presence of uniform mottling throughout the whole of both lung fields and a shadow just below the right hilar region (Figure I). In the opinion of the radiologist the mottling was almost certainly due to subacute miliary tuberculosis, while the infrahilar shadow was interpreted as indicating pneumonic consolidation.

On account of the severe and long-standing pain in the back the patient's spine was also radiologically examined and radiographs showed pronounced destruction of the body of the eleventh thoracic vertebra with some destruction of the intervertebral disk between the eleventh and twelfth thoracic vertebræ; the lumbar part of the spine, the sacro-iliac joints, the hip joints and the lines of the psoas muscle appeared normal. These observations were confirmed at a subsequent examination of the spine on July 11, 1941, and the changes in the vertebræ, like those in the lungs, were reported as probably tuberculous.

In spite of all these findings the signs of toxæmia, as gauged by the temperature curve and the leucocyte count, were not pronounced. The patient's temperature was as a rule normal, varying between 97° and 98·4° or 99° F., and often it was subnormal; indeed, between her admission to hospital and her death on August 12, 1941, there were only four isolated occasions on which the temperature rose as high as 101° F., and the only significant abnormality in the temperature curve was an increase in the diurnal variations over short periods, the maximum temperature remaining within normal limits. Examination of the blood revealed an absence of leucocytosis (the white cells numbered 6,000 to 7,000 per cubic millimetre), and no abnormality in the relative proportions of the white cells until just before death.

The main feature of the patient's clinical condition during her stay in hospital were increasing severity and radiation of pain, repeated hæmoptyses, progressive anæmia, weakness and loss of weight and finally respiratory embarrassment. The pain, which was at first confined to the lower part of the thorax posteriorly, was later felt in the lumbar region and hips and in the shoulders. Between the patient's admission to hospital and her death the sputum was almost continuously blood stained, frequently containing clots, although large amounts of blood were not brought up at one time. The blood was bright red and frothy and never took on a "prune juice" appearance. Over the same period the sputum was repeatedly examined for tubercle bacilli microscopically (on ten separate occasions) by cultural methods and by guinea-pig inoculation with negative results. Microscopic examination merely revealed the presence of polymorphonuclear pus cells and various cocci, while no elastic fibres were seen.

Blood examinations revealed the presence of a gradually increasing anæmia of orthocytic type, the number of red cells falling from about 5,000,000 to 4,000,000 per cubic millimetre, and the hæmoglobin value from 12·4 grammes per hundred cubic centimetres (85%) to 9·3 grammes per hundred cubic centimetres (64%), while the colour index varied from 0·86 to 0·78. The sedimentation rate was increased and varied from 15 to 17·5 millimetres per hour.

The pulse rate was increased out of proportion to the temperature, and varied between 85 and 100 beats per minute. Although the respiratory rate was increased to 20 to 25 respirations per minute, the respiration to pulse ratio remained normal—namely, about 1:4.

Towards the end of her illness (July, 1941) the patient developed a bed sore which added to her discomfort and probably caused a certain amount of toxæmia. Towards the end of June, 1941, a pleural effusion appeared on the right side and gradually increased in extent. Severe dyspnœa, accompanied by rapid shallow breathing, a rise of temperature and the appearance of œdema of the feet, marked the terminal phases of the patient's illness.

About ten days after the patient's admission to hospital, and after the first radiological report had become available, Dr. Steel asked me to examine the patient, since the question had arisen whether she was suffering from tuberculosis, from the Besnier-Boeck-Schaumann syndrome or from some other condition. The following further observations bearing upon this question may now be recorded.

No cutaneous eruptions were visible, nor was there any history of a rash. There was no enlargement of the superficial lymph nodes nor of the spleen and liver. The Mantoux test produced a positive reaction. The blood protein content was 6·3 grammes *per centum* and there was no disturbance of the albumin-globulin ratio, the albumin content being 4·3 grammes *per centum* and the globulin content 2·0 grammes *per centum*. X-ray examination of the hands and feet revealed no osseous lesions. On inspection of the radiograph of the chest it appeared that the mottling was rather coarser than that seen in miliary tuberculosis, and in this respect more closely resembled that sometimes observed in the Besnier-Boeck-Schaumann syndrome. The opinion of the radiologist was sought regarding this point, and also on the question whether the shadows seen at the hilum and below and external to it could be caused by enlarged hilar glands with an area of collapse below them. The radiologist concurred in the opinion that the character of the mottling was against a tuberculous lesion and in favour of the Besnier-Boeck-Schaumann syndrome or possibly lipoid histiocytosis. The report also stated that the dulness below and external to the hilum might be due either to the lesion's becoming confluent or possibly to localized atelectasis. As the condition progressed, however, later radiographs revealed the presence of an effusion at the base of the right lung, a considerable increase in the subhilar shadow, and finally a pronounced decrease in lung translucency involving the upper third of the right lung field (Figure II). These changes, taken in conjunction with the further evidences of erosion and anterior wedging of the eleventh dorsal vertebra, caused the radiologist to revert to the former view that the condition was tuberculous and that the more recent shadows in the lung were due to consolidation, while the mottling was probably due to subacute miliary tuberculosis.

In order to obtain further information regarding the source of the bleeding and especially with a view to seeing whether anything resembling sarcoids of the mucous membranes of the respiratory passages could be observed, an examination of the respiratory passages including bronchoscopic examination was undertaken. This examination was carried out on June 25, 1941, by Dr. H. M. Rennie, who reported as follows:

> The mucous membrane of the trachea and left bronchus was studded with small vesicle-like nodules, pale in appearance and without a tendency to hæmorrhage. The bifurcation of the trachea appeared abnormal; the anterior two-thirds of the carina was bulging and the posterior third thin and knife-like. There was marked narrowing of the right bronchus just below the origin of the upper lobe bronchus and extending for about one inch, beyond which level the bronchus appeared normal in diameter. The narrowed area was hard, granular, irregular, and bled very easily on manipulation. It was not possible to obtain material for a biopsy.

In spite of all these observations the diagnosis still remained in doubt. The condition present seemed difficult to reconcile with a diagnosis of either the Besnier-Boeck-Schaumann syndrome or tuberculosis, although it had more in common with the latter condition, especially if one kept an open mind on the subject of *granulie froide* in the sense employed by French physicians, implying tuberculosis. Bronchial carcinoma was regarded as an improbable diagnosis in view of the bilateral and disseminated character of the lesions in the lungs and respiratory tract.

Autopsy Report.

At autopsy, performed on August 14, 1941, 24 ounces of dark, straw-coloured fluid were found to be present in the right pleural cavity. Much of the right lung was collapsed. Many small nodules of newgrowth were present under the pleura, and some fine white lines probably of carcinomatous permeation were evident. On section numerous white nodules were seen scattered throughout the lung, with the exception of an area at the apex, which was the seat of a hæmorrhagic infarct. These nodules were more numerous in the lower lobe and most of them were rounded and varied in diameter from one millimetre to one centimetre. In the right hilar region and involving part of the lower lobe of the right lung there was an area of newgrowth considerably more extensive and less regular in outline than were seen elsewhere in the lung (see Figure III), and some submucous nodules were also seen in some of the larger bronchi in this region.

The left pleural cavity contained only a few ounces of fluid. In the left lung numerous nodules of newgrowth were evident, and under the pleura lines of lymphatic permeation similar to those seen in the right lung could be seen (see Figure IV).

The hilar lymph nodes were large and neoplastic, and several hard nodules of newgrowth were present in the neck. In the right side of the anterior part of the mediastinum there was a large, hard, neoplastic mass.

About two ounces of clear fluid were present in the pericardial cavity. The right auricle was dilated with post-mortem clot, and the right ventricle was dilated and hypertrophied. The left side of the heart appeared normal, and there was no aparent abnormality of the heart valves.

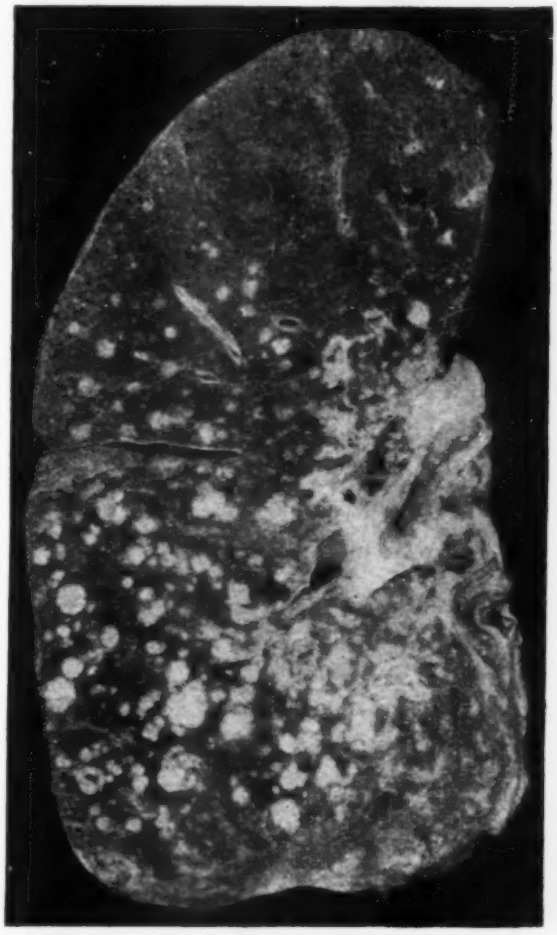

FIGURE III.

Cut surface of the right lung, showing the newgrowth in the right hilar region in relation to the bronchi and extending into the lower lobe.

In the ascending colon, a flat neoplasm measuring three centimetres by two centimetres in area showed superficial ulceration. The remainder of the alimentary tract was free from newgrowth. In the substance of the right ovary there was a single solid neoplastic nodule about 2·5 centimetres in diameter, which almost completely replaced the gland. The left ovary contained no newgrowth. The liver was affected by fatty degeneration and contained several scattered nodules of newgrowth, the largest of which were about two centimetres in diameter. The larger nodules were soft and hæmorrhagic in the centre. The left kidney contained a few small areas of newgrowth, but none was apparent in the right kidney. The body of the eleventh thoracic vertebra was somewhat collapsed, and a nodule of newgrowth was

present on the inner surface of the sixth left rib. The spleen, pancreas and adrenals contained no newgrowth.

Histological examination of the lesion in the hilar region of the right lung revealed malignant epithelial newgrowth (see Figure V), which was widespread in the walls of the bronchi. There was much irregularity in size and shape of the malignant cells and a tendency to alveolar arrangement of these cells could be made out near the bronchial lumina. A short distance from the lumina, however, the cells of the newgrowth were seen to be tall and columnar for the most part, and they had a definite glandular arrangement, lining spaces in some of which mucin, as shown by mucicarmine

FIGURE IV.

Pleural surface of left lung, showing widespread nodules of newgrowth and white lines of subpleural lymphatic permeation.

preparations, could be seen. A tendency to papilliform arrangement could be distinguished in some areas. In the mucous glands and cartilage no significant change was detected. The hilar lymph nodes were replaced by glandular carcinoma. Here an outstanding feature was a papilliform arrangement of many of the cells lining glandular spaces (see Figure VI).

In the nodules seen with the naked eye scattered throughout both lungs was found newgrowth similar in cell type and arrangement to that seen in the more regular parts of the hilar growth. Many of the lymph channels of the lung, both those accompanying vessels and those situated subpleurally, could be seen to contain masses of cancer cells. The arteries showed no special deviation from normal.

In the tissue from the anterior part of the mediastinum carcinoma was present; it was glandular in type, but the cellular arrangement was less regular than that in the lungs.

The lesion in the colon was in the submucosa and extended peripherally in that layer under the mucous membrane. In the centre it had ulcerated, and there also carcinomatous cells had invaded the inner muscle coat. In structure it was a glandular carcinoma similar to that seen in the lung.

In a section of the nodule in the right ovary carcinoma, also of a glandular structure, was seen. The liver nodule examined had similar characteristics, and extreme fatty degeneration was also present. In a kidney nodule examined the cells were less regular in size, shape and arrangement than elsewhere. In the eleventh thoracic vertebra necrosis was widespread, but in the necrotic tissue ghost cell outlines of cancer cells were evident in an arrangement similar to that seen elsewhere.

The structure of this widespread newgrowth indicated that it had arisen from columnar epithelium; but the exact site of origin was uncertain. The isolated growths in liver, kidney and bone may be considered to be blood-borne metastases. The naked-eye appearance of the growth in the colon suggests metastasis, and the histological picture supports this view, since the growth appears to arise in the submucosa, and no malignant surface epithelium is to be seen. The naked-eye appearance of the ovarian growth suggests metastasis also—a solitary nodule in the substance of the ovary.

At autopsy the growth in the hilar region of the right lung appeared to be somewhat different from the other lesions seen scattered throughout the lungs; it was larger and more diffuse, and lay in close proximity to the bronchi. Serial skiagrams of the chest also revealed progressive consolidation in the right hilar region. Sections taken from this region, however, failed to give conclusive evidence regarding the primary site of the newgrowth. The histological appearances, however, were consistent with origin from bronchial epithelium, the presence of mucin suggesting origin from the bronchial mucous glands, and it is most likely that the growth arose primarily in the hilar region of the right lung.

Let us now consider the mode of spread within the lungs. It has been noted that the hilar lymph nodes were enlarged and carcinomatous. Also fine white lines of lymphatic permeation were seen under the pleura at autopsy. Histologically many lymph vessels, both subpleural and perivascular, were seen to contain masses of carcinomatous cells.

It is generally believed that lymphatic spread in the lungs is due to blockage of the hilar glands causing retrograde permeation of the lymphatics. Willis[40] points out that blockage of lymph channels by tumour growth within the lung itself will divert the flow of lymph, and so aid this process. It is probable that in this case lymphatic spread was the chief factor in the wide dissemination of the tumour within the lungs.

However, isolated metastases considered to be blood-borne were present in the liver, kidney and bowel, so that it is possible that tumour cell emboli passed into the bronchial arteries, causing blood-borne metastases in the lungs; but histological evidence in favour of this is lacking. The occurrence of multiple pulmonary metastases from tumour cell emboli reaching the blood stream from the involved hilar lymph glands by way of the thoracic duct has been suggested by Ziegler;[41] but this mode of spread was not evident in this case.

At the periphery of the hilar lesion and of some of the scattered pulmonary lesions, direct intraalveolar spread was to be seen, the cancer cells actually appearing to grow along the alveolar walls in some areas. However, this would not produce the many isolated nodules of growth seen throughout the lungs.

Although the appearance of the lungs may be considered to have been produced by widespread lymphatic permeation, the pathology varies in two main respects from the majority of those cases previously reported. First, generalized lymphatic carcinoma in the lungs in many of such cases reported has followed primary gastric carcinoma. In the present case no newgrowth was detected

in the stomach. Secondly, changes in the arteries were by no means an outstanding feature, and evidence of obliterative endarteritis mentioned by Girode[38] in 1889 and reported more recently by von Meyenburg[39] (cited by Schwarzmann[20]), by Greenspan[13] and by Wu[40] was lacking. However, dilatation and hypertrophy of the right side of the heart, also described by these authors, were evident at autopsy.

Diagnosis.

This case presents an interesting diagnostic problem. Without a post-mortem examination, it is probable that the case would have been recorded as one of tuberculosis. In agreement with a diagnosis of tuberculosis the following points may be cited: the history of a chronic cough with hæmoptysis, loss of weight and night sweats; destruction of the eleventh thoracic vertebra; pleural effusions; the appearance of miliary lesions and also shadows suggestive of consolidation seen on radiological examination; positive Mantoux reaction, increased blood sedimentation rate, and anæmia. Furthermore, the patient had been under observation for some months at the tuberculosis clinic of the Royal Prince Alfred Hospital, and this might have raised a certain presumption in favour of tuberculosis, influencing subsequent diagnostic opinion. On the other hand, certain facts had to be weighed against those just mentioned. In spite of what looked like miliary lesions and extensive consolidation in the lungs and a gross progressive osseous lesion in the spine, the course of the disease was prolonged and accompanied by little, if any, pyrexia. There was neither a polymorphonuclear leucocytosis nor a leucopenia (with relative increase in polymorphonuclear cells), such as occur in acute miliary tuberculosis, nor did the differential leucocyte count show a shift to the left or any change in the relative proportions of monocytes and lymphocytes as may be seen in the more chronic forms of tuberculosis. Again, the sputum was never abundant, in spite of a chronic cough, and all attempts to demonstrate the presence of tubercle bacilli yielded negative results. The hæmoptysis was not typical, in that it was a more or less continuous hæmorrhage; at all events, this was so during the period of the patient's stay in hospital, although if the patient's statement is to be relied upon, she did on one occasion, prior to her admission to hospital, bring up as much as half a cupful of blood at one time. The miliary lesions in the lungs were also coarser than those usually seen in miliary tuberculosis, although in the earlier radiographs they were small enough to make the differentiation difficult. The swellings and narrowings of the lumen of the trachea and bronchi seen on bronchocopic examination did not suggest tuberculous lesions, although the smaller nodules might have been mistaken for tubercles. If the lesions in the trachea and bronchi had been tuberculous, one would rather have expected to find tubercle bacilli in the sputum; but this does not, of course, necessarily follow. Finally, there was nothing in the patient's previous health, family history or personal environment pointing to tuberculosis.

With regard to the Besnier-Boeck-Schaumann syndrome, certain points of resemblance may be put forward. There was the presence of rather coarse miliary lesions in the lungs of a patient showing little if any pyrexia. Radiographs of the lungs even revealed some of the marbling seen in the Besnier-Boeck-Schaumann syndrome; but whereas in that condition the marbling is probably due to the invasion of the interlobular septa and peribronchial and perivascular lymphatics by granulomatous tissue, in this case it was due to permeation of the lymphatics with carcinoma cells (Figure I). Again, enlarged hilar glands are very commonly seen in the Besnier-Boeck-Schaumann syndrome, and these may sometimes compress the bronchi and cause areas of collapse below them. A somewhat similar appearance was seen in radiographs taken at an early stage in this case (Figure I). At post-mortem examination it was found that the hilar glands were enlarged owing to carcinomatous invasion, while the lung below was infiltrated.

A chronic cough with very little sputum may be due to sarcoids in the respiratory passages, and the nodules seen at bronchoscopic examination might conceivably have been mistaken for sarcoids. Although changes in the leucocyte count and the plasma proteins may occur in the Besnier-Boeck-Schaumann syndrome, an absence of such changes is compatible with the presence of miliary lesions in the lungs in that disease. The sedimentation rate may be normal or it may be increased, just as in this case. The condition found in this case, however, presents many features which differ from those seen in the Besnier-Boeck-Schaumann syndrome. Among these are the following: the rapid downhill course of the illness in the last few months, the coarseness of the nodules in the lungs in the later stages (Figure II), the presence of pleural effusion and evidence of consolidation or of the confluence of lesions in the lungs; the absence of characteristic changes in the bones of the extremities, but the presence of a single gross lesion (without any of the characteristic features of sarcoidosis) in the eleventh dorsal vertebra; severe pain of wide radiation; and finally, the absence of any characteristic lesion in the lymph nodes, skin, eyes, *et cetera*. It is also usual in the Besnier-Boeck-Schaumann syndrome for the response to the tuberculin test to be negative, although this is not invariable. While sarcoids in the respiratory tract may cause some hæmorrhage, there is no record, as far as I have been able to ascertain, of such severe, continuous and prolonged hæmoptysis as in this case.

In many respects the clinical features of the case might have suggested the presence of a pulmonary neoplasm—namely, a pleural effusion, diffuse shadows in the lungs seen on X-ray examination, enlarged hilar glands and swellings obstructing the bronchi seen on bronchoscopic examination, the early onset of severe and widely radiating pain, destruction of the eleventh thoracic vertebra suggesting metastasis, the occurrence of hæmoptysis and of cough without sputum in the early stages, absence of tubercle bacilli in sputum, the relatively apyrexial course, and the presence of wasting and anæmia. On the other hand, the bilateral, widespread and more or less even distribution of miliary lesions, as seen on radiological examination, together with the numerous small vesicle-like nodules seen on bronchoscopic examination, were against any of the ordinary types of pulmonary neoplasm, whether primary or secondary. The pleural effusion contained no blood, and the sputum never had the characteristic prune-juice appearance; but not much weight could be attached to these negative features.

Acute miliary carcinomatosis of the lungs usually runs a rapid course of seldom over two months from the appearance of the first symptom; but in this case the duration of symptoms extended over more than a year, although the illness, after a pronounced exacerbation of symptoms, ran a rapid downhill course during the last four months. The most probable interpretation of these findings is that the condition began as one of bronchial carcinoma of rather a slow-growing type, but that about April, 1941, there was a sudden eruption of secondary foci in the hilar lymph nodes leading to an invasion of the lymphatics of both lungs which caused disseminated lesions in all lung fields and was accompanied by an aggravation of the symptoms. The fact that the patient lived for four months after this event suggests that the development of the secondary deposits in the lungs was slower than is usual in generalized lymphatic carcinomatosis. This relatively slow progress may be correlated with the development of coarse granulation and ultimately with the appearance of nodules, some of them fully the size of a hazel nut, whereas an examination of previous records would point to the conclusion that in the most acute cases granulation is at a minimum, while radiographs show strand-like shadows radiating out from the hilum, caused by distension of the lymphatics with carcinoma cells. In this case the strands, coarser near the hilum and becoming more attenuated towards the periphery, were also in evidence, but were not so pronounced as in the acute cases reported, for example, by Costedoat[12] and Schwarzmann.[20] The granules or nodules occurred at intervals along these strands, apparently at points where branching occurred, giving the appearance of pearls on a

string; the largest were seen at the hilum, while they diminished in size towards the periphery.

Among other conditions which rarely cause *granulie froide* and would have to be considered in arriving at a diagnosis in such cases are lymphogranulomatosis, pneumonokoniosis, mycotic diseases of the lungs, especially blastomycosis, miliary hydatid disease, chronic disseminated peribronchial tuberculosis, multiple minute bronchiectases following chronic bronchitis, disseminated leuchæmic foci, disseminated minute gummata, lipoid histiocytosis, some cases of passive pulmonary congestion and lipiodol injection. It is unnecessary to enter into any detailed discussion regarding these; suffice it to say that a careful history, examination of the sputum, examination of the blood (including cholesterol content), X-ray examination, special tests such as the Casoni reaction, and the search for evidences of the disease in question in other parts of the body, would help to establish the diagnosis in doubtful cases.

Those cases of generalized lymphatic carcinomatosis of the lungs in which cyanosis is a feature, may have to be differentiated from pulmonary artery thrombosis with Ayerza's syndrome (see case reported by Montgomery[20]). Common to the two conditions are severe dyspnœa, cyanosis, hypertrophy of the right side of the heart, chronic venous congestion, cough and hæmoptysis, while the history may extend over a few months. In Montgomery's case also slight anæmia was present, although erythrocytosis is the rule in Ayerza's syndrome. Patients suffering from generalized lymphatic carcinomatosis probably seldom exhibit the intense purple cyanosis characteristic of Ayerza's syndrome, while the presence of characteristic radiological findings may assist in the diagnosis.

Discussion.

Inasmuch as granulation is not an invariable feature of generalized lymphatic carcinomatosis (cancerous lymphangitis) of the lungs, it is apparent that miliary carcinomatosis (or carcinosis) is only a special form of that condition.

History.

The earliest description of generalized lymphatic carcinomatosis of the lungs was given by Raynaud,[32] who in 1874 described a diffuse invasion of the lymphatics of the lungs without the appearance of cancerous nodules of any importance in the parenchyma. In the same year Troisier[29] published a thesis on pulmonary lymphangitis, in which he recorded the known cases, and soon after this Hillairet[26] reported two cases.

The most important early contribution to the pathology of the condition, particularly with reference to the mode of cancerous invasion of the lungs, was that by Girode[16] in 1889, while twelve years later Troisier and Letulle[28] (1901) extended our knowledge of its histology, demonstrating the distension of the lymphatic channels by proliferating carcinoma cells.

Further notable contributions to the pathology were made by Bernard and Cain[6] (1913), who gave an illustration showing a blood vessel surrounded by a ring of distended lymphatics and described the interstitial and parenchymatous reaction in the lung, pointing out the absence of invasion of the alveoli. Later, Meyenburg[23] (1919) drew attention to the compression of the smaller bronchi by peribronchial and perivascular infiltration and the occurrence of endarteritis of the blood vessels in the vicinity of invaded lymphatics. Bard,[4] in 1906, described the essential clinical features of the condition and discussed the differential diagnosis. Since then, additions to our knowledge have been made by other clinical observers and by radiologists,[3][10][11][17][18][22][24][25][33][34] notably Weil,[35] Lorenz,[27] Assmann,[2][3] Lucas and Pollack,[21] and Schwarzmann.[31]

Age.

The age of onset is rather earlier than that of most cases of carcinoma, the highest incidence being in the third decade.

Primary Focus.

In the majority of cases the primary focus is in the stomach, and a noteworthy feature is the frequency with which it has been latent; this has caused it to be overlooked clinically. Consequently the patient may come under observation for pulmonary symptoms while his general condition yet remains good. Other sites for the primary focus have been the bronchi (Ziegler,[42] Schwarzmann,[30] Assmann[2][31]), the skin (Blum[7]), the uterus (Costedoat[12]), the kidney (Levai[20]), the ovaries (Moretti[31]) and the tongue (Ewing[14]).

Symptoms and Signs.

Costedoat[12] has described what he regards as prodromata, lasting about fifteen days up to four or five weeks and consisting of a vague change in the general state (probably corresponding, in his view, to the development of the unknown humoral or tissue factors responsible for the irruption of the cancer cells into the pulmonary lymphatics) followed by loss of weight, often considerable weakness, and anorexia.

The characteristic symptoms of the disease are dyspnœa, cough with little if any expectoration, small hæmoptyses, pain in the side and night sweats; examination of the chest in the early stages reveals either no abnormality or only a few scattered râles or modified breath sounds and possibly pleuritic friction; the pulse and the respirations are accelerated, but the temperature remains normal or only very slightly elevated.

Nearly all authors stress the importance of dyspnœa as a pronounced and constant feature. It may be slight at first, but rapidly becomes severe and permanent. It may be the earliest and in some cases the only symptom. On the other hand, in the case above reported, severe dyspnœa did not occur until the later stages, and dyspnœa was preceded by cough, hæmoptysis, pain and weakness even after the general exacerbation of the symptoms had occurred. Among the factors responsible for the dyspnœa, the following may be mentioned: narrowing of the vascular bed and compression of the smaller bronchi, rigidity of the lungs, pulmonary œdema, and pleural effusion; the condition would be aggravated by anæmia. Cyanosis is a less common feature and may be obscured by anæmia. Venous congestion and in some cases perhaps imperfect oxygenation of the blood passing through the lungs may be responsible for it.

The hæmoptysis takes the form of small repeated hæmorrhages; rarely are large amounts of blood brought up at one time. Apart from the development of special signs due directly to the further evolution of structural changes in the chest, the clinical findings in the case here reported were those of progressively increasing anæmia, orthocytic in type, and œdema of the lower extremities, due probably to a combination of anæmia and raised venous pressure caused by obstruction in the pulmonary circuit. No direct estimation of the venous pressure was made, but the dilatation and hypertrophy of the right side of the heart found at post-mortem examination would point to there being some obstruction in the pulmonary circulation, although histological examination of the lungs revealed no evidence of the obliterative endarteritis described by Meyenburg,[23] Greenspan[13] and Wu.[41] Among negative findings of importance were the absence of leucocytosis or of changes in the maturity or proportion of the white cells, and the absence of tubercle bacilli in the sputum.

Radiology.

In contrast to the relative paucity of physical signs in the chest, radiological examination revealed the presence of extensive lesions. The hilar shadows were increased and appeared sharply defined, while the lung fields were traversed by a mesh of strands emanating from the hilar region and becoming more attenuated as they reached the periphery, where they merged into a fine network. These strands are the radiological expression of the permeation of the peribronchial, perivascular and subpleural lymphatics by cancer cells. In the earliest stages there is only a slight marbling of the lung fields, and as the shadows become more pronounced there may be an appearance of very fine granulation—finer than that seen in pulmonary tuberculosis—where the shadows of the strands are superposed and cross one another. In some cases—apparently the more acute types—the strands con-

tinue to become broader and denser, with little if any further increase in the granular appearance. In others there is little further increase in the density of the strands, but granules definitely appear; they are not to be accounted for by superposition, but are due to the local deposit and growth of cancer cells at intervals along the course of the lymphatics, apparently at the points where branching takes place. The nodules appear in almost rectilinear or gently curved chains along the strands, the larger ones being situated towards the hilar region, while they decrease in size towards the periphery, the appearance resembling that of a chain of pearls. In the case here reported serial X-ray films showed a progressive increase in the size of the individual nodules, and eventually a few larger independent masses appeared (Figures I and II). As a rule, the nodules are larger and more closely packed in the lower two-thirds than in the upper third of the lung fields. In this respect, and with regard to the appearance of strands, the distribution of lesions resembles that seen in the Besnier-Boeck-Schaumann syndrome, but the nodules in miliary carcinomatosis may ultimately become much larger than those in the former syndrome. On the other hand, they are much smaller (rarely exceeding the size of a hazel nut), more numerous and more regular in their arrangement than those occurring in ordinary secondary carcinoma. In ordinary secondary carcinoma shadows cast by invaded lymphatics may sometimes be seen, but instead of emanating from the hilum they radiate from the individual nodules and do not pass from one nodule to another. Ordinary secondary carcinoma is also much slower in its evolution.

The interesting question arises of why secondary carcinomatosis of the lungs should take sometimes the miliary and sometimes the larger nodular form. Is it due to some peculiarity of the cancer cells themselves? Or is it possible that previous (tuberculous?) disease or sensitization of the hilar glands may be a factor in determining the breaking up of secondary deposits in these glands and the sudden and massive irruption of cancer cells into the pulmonary lymphatics? The existence of tuberculous foci may be difficult to determine in glands already invaded by carcinoma, and no evidence of tuberculous lesions could be demonstrated in the case here reported. Costedoat and Codvelle[11] have described a case of miliary carcinomatosis of the lungs in a subject in whom tuberculosis had been diagnosed a year previously; but a similar diagnosis had been made in the case of our patient, who had attended the tuberculosis clinic for several months.

Types of Generalized Lymphatic Carcinomatosis of the Lungs.

From the records of previous cases and our own, it may be concluded that we can distinguish two main types of generalized lymphatic carcinomatosis of the lungs: (i) a diffuse or non-granular type; (ii) a miliary (granular or nodular) type. The first of these runs an acute course and is marked by a dense network of strands, with little if any evidence of granulation. The second is somewhat slower in its evolution; the network is inconspicuous, but miliary lesions are much in evidence. There are probably all transitions between the two types. If no obvious network is seen, and if there are no increased hilar shadows, but disseminated miliary lesions are present, a blood spread of secondary carcinoma and not generalized lymphatic carcinomatosis might be suspected. Such cases have not been clearly differentiated; but cases reported by Blum[7] (chorionepithelioma) and Eizaguirre[12] may possibly fall into this category.

Course and Prognosis.

Generalized lymphatic carcinomatosis of the lungs as a rule runs a rapid course, seldom of more than two months' duration, although in the present case it was established that it had existed for at least four months. Death appears to be due to asphyxia and right-sided cardiac failure. It supervenes in a paroxysm of dyspnœa, or it may occur suddenly. The interval between the appearance of dyspnœa and death may not exceed a few days, but it may be a month.

Summary and Conclusions.

1. The clinical, radiological and pathological features of generalized lymphatic carcinomatosis of the lungs are described and discussed.

2. Two types, diffuse and miliary, have been differentiated.

3. Attention is drawn to the importance of the miliary type as a cause of the syndrome of *granulie froide*.

4. A case of miliary type is recorded, together with an autopsy report, and the differential diagnosis and pathogenesis are discussed.

Acknowledgements.

We wish to express our thanks to Dr. R. S. Steel for the opportunity of studying this case, to Professor Keith Inglis for his help and criticism in connexion with the histological investigation, and to Mr. Woodward Smith for the illustrations.

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THE KLINEFELTER-REIFENSTEIN-ALBRIGHT SYNDROME.

By H. F. BETTINGER and BRUCE ROBINSON.
Melbourne.

THE medical examination of large numbers of healthy young men during this war has again shown that gynæcomastia is not so rare as it is sometimes assumed to be. A definite though slight increase in the size of the breasts is so common among boys during puberty that it has to be regarded as physiological. In the majority of cases this swelling regresses after some time, but occasionally it persists or even increases. Although it is usually the only pathological feature in an otherwise perfectly healthy young man, it may have rather serious repercussions by debarring him from participation in many kinds of sport and creating embarrassing situations in the use of common washrooms, as in the army or in factories and so on. Nevertheless, except for the few cases in which it was obviously the result of a tumour of the testis, adrenal or pituitary, the condition has been regarded more as an anomaly than as a disease, and as one creating at most psychological problems. It is therefore of great interest that in 1942 Klinefelter, Reifenstein and Albright showed that gynæcomastia might be one factor only of a syndrome of which the other components were of far greater importance. Last year Heller and Nelson went a step further by concluding from the analysis of twenty cases that gynæcomastia was not even an essential factor in this new syndrome. What, then, are the cardinal features of this syndrome?

The Syndrome.

The syndrome is composed of a number of constant as well as variable features. The constant features are the following: severe degeneration of the testis, which involves predominantly the seminiferous tubules, but to a much smaller degree or not at all the interstitial cells of Leydig, and a disturbance of the endocrine equilibrium which manifests itself most clearly by an increase in amount of gonadotrophic hormone excreted in the urine. The variable features concern the general body configuration and the development of the external genital organs, as well as that of the secondary sex characteristics, including gynæcomastia.

On the basis of these variable features Heller and Nelson have distinguished three subgroups: the eunuchoidal, the moderately eunuchoidal and the normal. In the first group the skeleton is of eunuchoidal proportions, the external genitalia are infantile, erections occur but not ejaculations, the pitch of the voice is high, muscular development is poor, axillary and pubic hair is delayed in development and scanty. Gynæcomastia is not a regular or prominent feature. In the third group (Heller and Nelson's term "normal" may be misleading and is better replaced by "non-eunuchoidal"), body configuration, external genitalia and secondary sex characteristics do not show significant deviations except for the usually pronounced gynæcomastia. The second group obviously comprises intermediate stages. All the three groups have in common the "constant" features—that is, the testicular lesions and the endocrine disturbances.

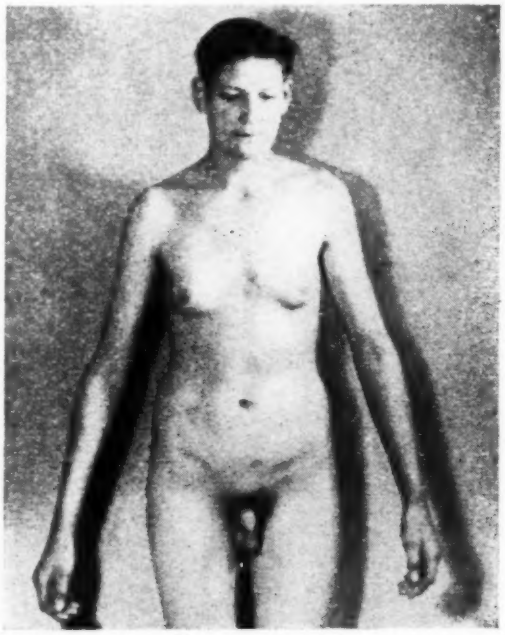


FIGURE I.
The patient before removal of the breasts.

Heller and Nelson have stated that cases of this kind are by no means rare. The twenty cases that form the basis of their papers have been collected within twelve months; during the same period a further thirty cases were seen, but as they could not be studied completely, they were not included in the analysis.

The case that will be described presently is the first and only one that has been recognized here as belonging to the new syndrome; but we feel justified in drawing attention to the syndrome, as not only is it of great scientific interest, but also it has important practical implications.

Report of a Case.

E.S. first attended Dr. R. McMeekin's medical out-patient clinic at the Royal Melbourne Hospital on March 24, 1945, with the complaint of bilateral enlargement of the breasts.

ILLUSTRATIONS TO THE ARTICLE BY PROFESSOR C. G. LAMBIE AND Dr. J. COLLIER.

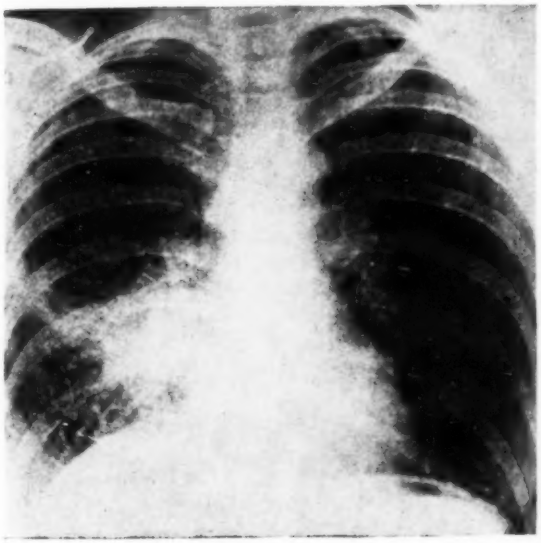


Figure I.

Skiagram of the thorax taken on May 22, 1941, showing hilar and subhilar shadows; strands radiating from hilum and chains of shadows cast by miliary lesions along the strands.

Figure II.

Skiagram of the thorax taken on July 10, 1941, showing increase in size of miliary lesions as compared with those shown in Figure I, and the appearance of larger nodules; pleural effusion on the right side and a decrease in lung translucency in the upper third of the right lung field.

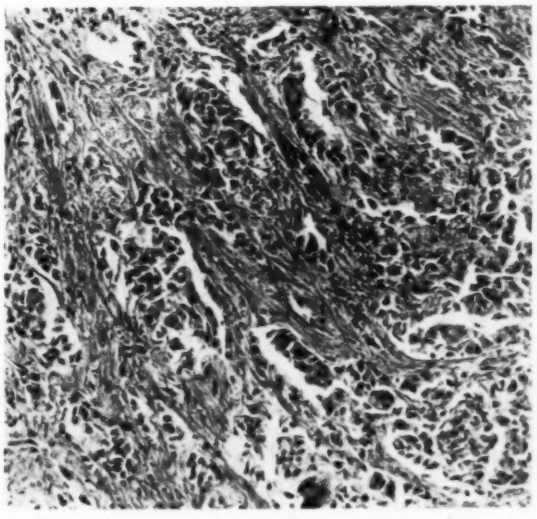


Figure V.

Photomicrograph showing the newgrowth in the wall of the right bronchus (× 120).

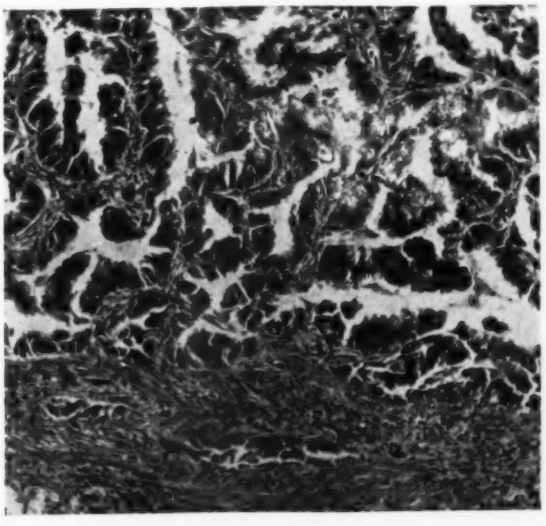


Figure VI.

Photomicrograph showing the papilliform arrangement of the newgrowth replacing a hilar lymph node (× 100).

ILLUSTRATIONS TO THE ARTICLE BY Dr. H. F. BETTINGER AND Dr. BRUCE ROBINSON.

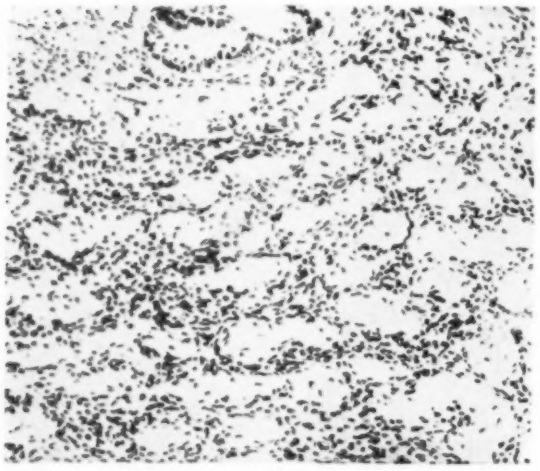
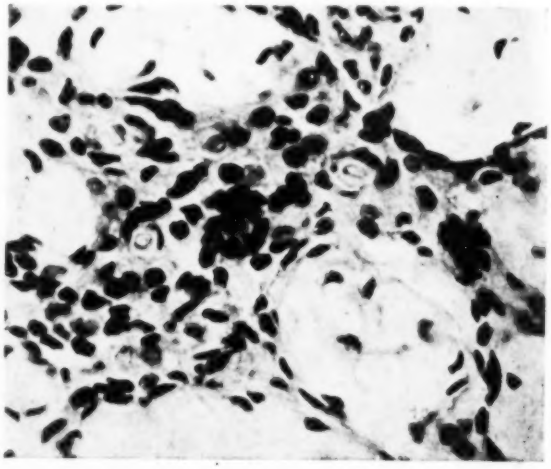


FIGURE III.



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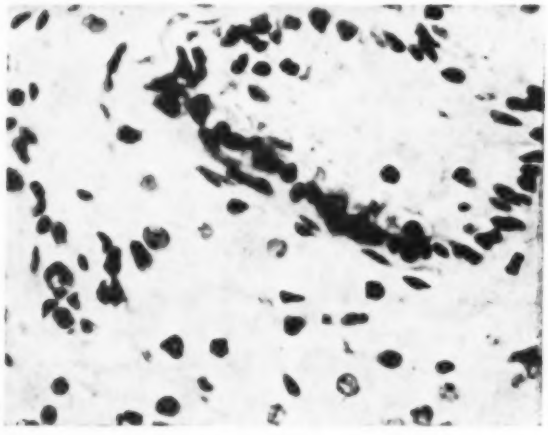

FIGURE V.

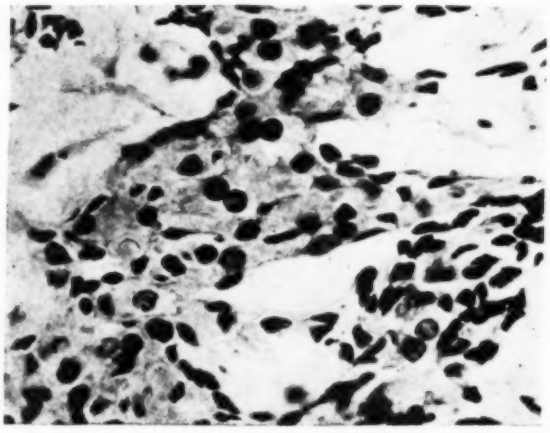

FIGURE VI.

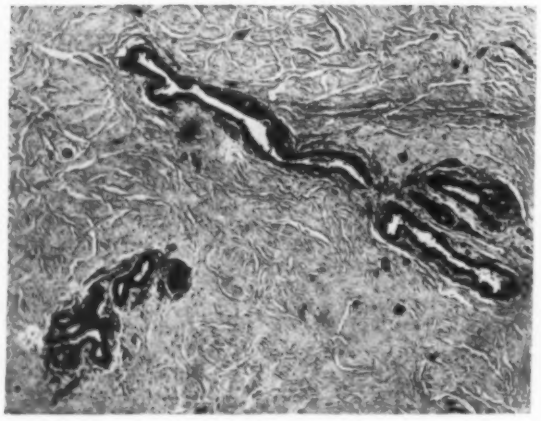

FIGURE VII.

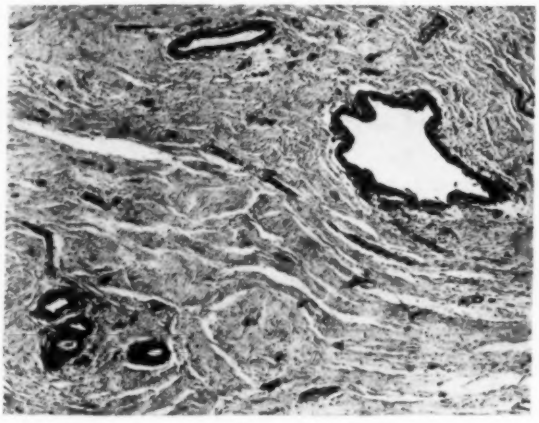

FIGURE VIII.

ILLUSTRATIONS TO THE ARTICLE BY Dr. T. M. GREENAWAY, Dr. J. K. MADDOX, Dr. B. T. EDYE, Dr. E. M. DAY AND Dr. J. S. ROBERTSON.

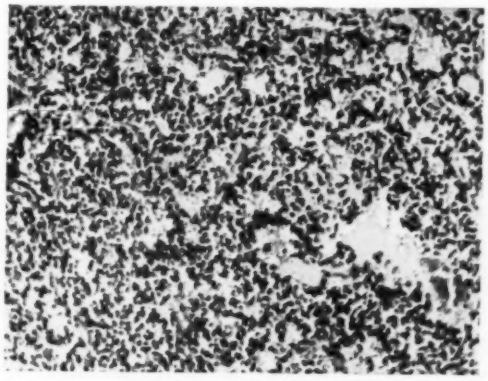

Figure II.—Tumour IA (× 100).

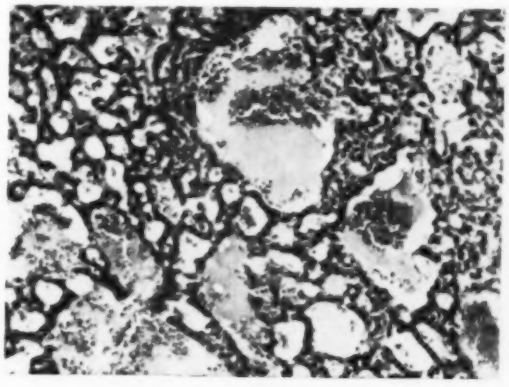

Figure IV.—Tumour IB (× 100).

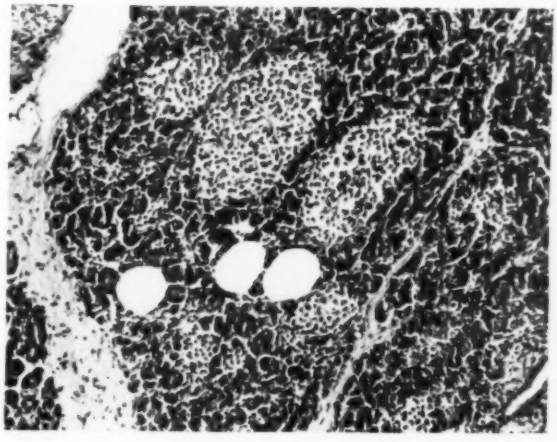

Figure V.—Pancreas adjacent to tumour IB (× 100).

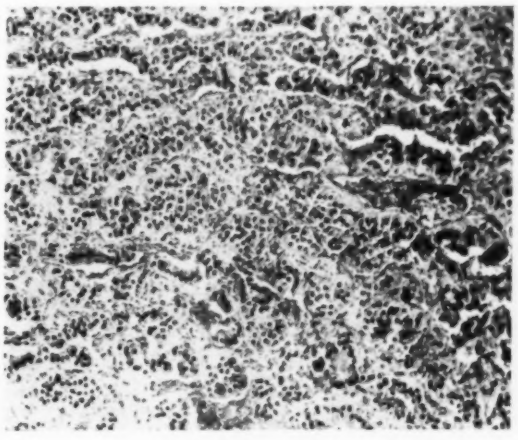

Figure VII.—Tumour II (× 100).

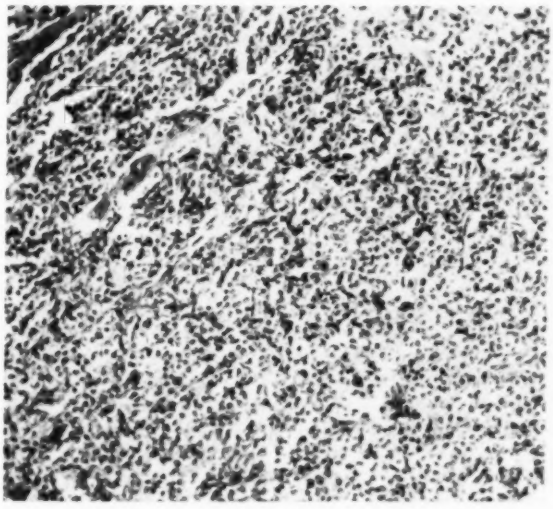

Figure VIII.—Tumour II (× 100).

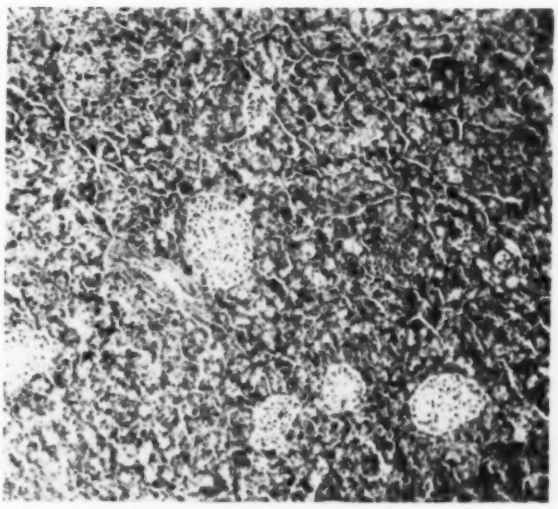

Figure IX.—Pancreas adjacent to tumour II (× 100).

ILLUSTRATIONS TO THE ARTICLE BY Dr. E. GRAEME ROBERTSON.

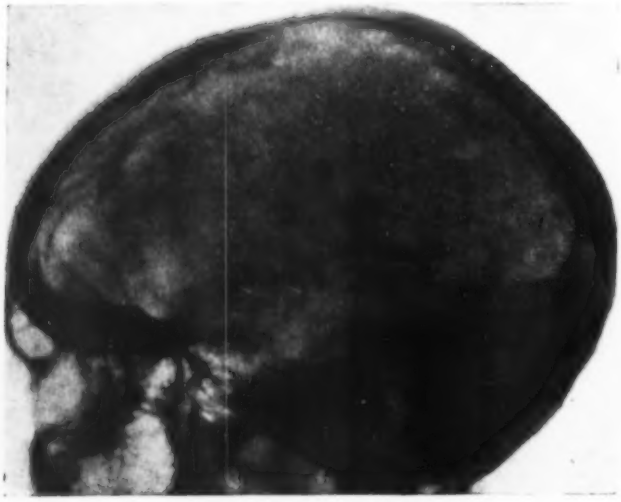

FIGURE IIA.
Radiograph of skull showing intracerebral calcification in the first patient, lateral view.

FIGURE IIB.
Radiograph of skull showing intracerebral calcification in the first patient, occipito-frontal view.

ILLUSTRATIONS TO THE ARTICLE BY Dr. RICHARD FLYNN.

FIGURE I.

FIGURE II.

His age was eighteen years and five months. During the preceeding eighteen months his breasts had developed female characteristics of size and contour. He was extremely sensitive about his peculiarity and wished for surgical treatment. He was persuaded to defer operation and to undergo investigation and a trial of medical treatment.

The patient was the third child of seven children of normal, healthy parents. There was no history of endocrine disturbance in any other member of his family. He had an average school record and left school at the age of fourteen years. He had since done unskilled work in a pottery. Apart from appendicitis with peritonitis, he had had no previous noteworthy illness. He had never suffered from mumps. He grew up amongst his brothers and sisters and enjoyed most of the same games, but was never physically "tough" or muscularly strong. Thus he went skating, but did not play football. He had never felt that his tastes and interests were different from those of his boy friends. He took only a mild interest in girls. He would have liked to dance, but was afraid of girls discovering his peculiar conformation. He had no particular girl friend. His mother stated that he was not effeminate, although he was slightly more dependent on her than the other boys of the family. His voice had never definitely broken and he had never shaved, but pubic hair appeared at the age of fourteen years. He had occasional erections and had nocturnal emissions every six or seven months. He had no complaint of polydipsia or polyuria and no headaches. At no time had any fluid been expressed from the nipples.

When first examined, E.S. was a tall, fair, beardless lad who was shy and reserved. His height was six feet one inch and his span six feet four inches. His voice was quiet and of high rather than low pitch, though it was not a true boyish alto. His frame was large, but his muscular development was poor. The contours of the limbs and body were not in general feminine, though his pelvis was rather broad for a male. Apart from his breasts, the distribution of the subcutaneous fat was normal for a youth of his build. His hands and feet were long and somewhat coarse. The nails of both index fingers were noticeably curved. The features of his face were fine and lacked obvious masculinity. The hair of his head was fair, fine in texture and straight. The only hair on his face was a fine lanugo. There was no body hair except a scanty growth in the axillæ, pubic and perineal regions. The pubic hair had the typical concave upper margin of the female. His skin was fair and fine in texture. "Goose flesh" appeared readily. A mid-line pigmented stria ran from the umbilicus to the pubis.

The breasts were moderately enlarged and somewhat pendulous. The left nipple was inverted; the right was not, but was larger than in the normal male. The nipples and areolæ were more pigmented than in a normal virgin breast. No fluid could be expressed from either breast. On palpation the breasts were shotty in texture. No accessory nipples or mammæ were present (Figure I).

The retracted penis measured three inches from the tip to the pubic arch. The foreskin retracted well and the meatus was normally placed. The bulb of the penis could be palpated in the perineum and appeared normal. The scrotum was not cleft. The testes were small and soft, but freely descended. The inguinal canals were clear. The prostate was small, but easily palpable rectally.

The larynx was not prominent. The thyreoid gland was soft and not enlarged. The liver was not palpable. The tongue was deeply fissured by multiple clefts, but was not sore.

The only other noteworthy clinical finding was the complete absence of all tendon reflexes, even with reinforcement.

The following investigations were made.

1. On September 5, 1945, a psychological examination was made by Dr. A. R. Phillips, of the Travancore Clinic, Flemington, to form an opinion of the patient's psychosexual organization, as at this time the possibility of intersexuality was being considered. The patient's intelligence was estimated by the revised Standford-Binet test. His chronological age was eighteen years and four months, and his mental age was thirteen years and eight months. His intelligence quotient was 91% (normal, 99% to 110%). His rating on a masculinity-femininity scale was estimated by a method adapted from Terman and Miles. The result was as follows:

> So far as the personality was sampled by the tests applied it was found to be masculine rather than feminine, but not strongly masculine. On the scale of sexual inversion derived from the M.-F. test no evidence of sexual inversion was found, i.e. he does not resemble in personality the typical male sexual invert on which the inversion scale is standardized.

Dr. Phillips's conclusions were that E.S. was of low normal intelligence, and that his psycho-sexual make-up was masculine, but not strongly so. On this point the psychometric tests confirmed the impression gained from the clinical examination. The personality type was appropriate to the physical findings, which seemed to point to a eunuchoid rather than a sexual intergrade.

2. A urinary androgens test showed that 1·3 milligrammes of 17-ketosteroids were excreted in twenty-four hours (normal for men, about four to ten milligrammes in twenty-four hours).

3. An X-ray examination of the skull revealed a normal *sella turcica*. The ocular fields and fundi were normal.

4. An X-ray examination of the wrists and elbows revealed no abnormality of epiphyseal fusion.

FIGURE II.
The patient after removal of the breasts.

5. An X-ray examination of the chest revealed no evidence of enlargement of the thymus gland.

6. The Wassermann and Kahn tests gave negative results.

7. The sugar tolerance was normal.

8. The basal metabolic rate was −15%.

Although at this stage a testicular biopsy had not yet been performed, and the result of estimation of the titre of the gonadotrophic hormone excreted in the urine was *sub judice*, there was no longer any doubt that the case was not one of intersexuality as first suspected, but a typical example of the syndrome described by Klinefelter, Reifenstein and Albright, and that the patient belonged to the moderately eunuchoidal group of Heller and Nelson. The state of the genital organs, the hair distribution, the general body build, the pitch of the voice, the gynæcomastia and the results of the investigations provided a sufficient number of Heller and Nelson's constant and variable features to make the diagnosis definite.

Treatment.

For extraneous reasons the testicular biopsy and the removal of the breasts had to be deferred.

Before the correct diagnosis was established, the patient was given weekly injections of 1·0 millilitre of "Antuitrin-S" (Parke, Davis and Company) from April 18 to October 26,

1945. In the light of the later diagnosis it was not surprising that no effect was observed on the general condition. However, during July he developed a painful cyst about one inch in diameter in the right breast. This lasted for three days and then gradually subsided. On November 2 treatment with methyl testosterone tablets, five milligrammes sublingually three times a day, was commenced. The result was dramatic. When he was examined one week later it was noted that his voice was fuller. He complained that he was having too many erections, and the dosage of methyl testosterone was reduced to two tablets a day, whereafter erections occurred only three or four times a day. He noticed that his urine became brown in colour. No other "toxic" effects were noticed. This treatment was continued until January 4, 1946, when the tablets became unobtainable. He noticed that erections continued for over three weeks in the absence of treatment. Testosterone implants were considered, but the materials were unobtainable. There seemed no object in giving injections, as the results from oral therapy were so satisfactory.

During the time when he was taking methyl testosterone his personality changed from that of an undeveloped eunuchoid to that of a normal young man, his conduct became much more assured and he was much less shy. He was observed to take an obvious masculine interest in the nurses. His voice became fuller, and even in this short period an occasional coarse hair appeared on his upper lip. He also developed *acne vulgaris* on the face during this time.

On January 14 Dr. G. R. A. Syme performed a bilateral mastectomy through subareolar semilunar incisions (Figure II). The glands were removed *en masse*. At the same time a small piece of the right testis was obtained for examination.

Histological Findings.

Examination of sections through the particle of testicular tissue shows that the majority of the seminiferous tubules are completely hyalinized. Only very rarely is a non-hyalinized tubule seen; but these never contain any seminiferous epithelium; they are lined by a single layer of Sertoli cells. As far as the very small size of the biopsy allows one to judge, the interstitial cells of Leydig are present in about normal numbers. However, their cytoplasm contains few or none of the granules which have been usually associated with functional activity (Figures III to VI). The breast tissue has a uniform structure; it consists mainly of dense fibrous tissue. Epithelial formations, which are not numerous, all have the appearance of ducts, and no development of alveolar tissue seems to have occurred (Figures VII and VIII).

Discussion.

An interesting point in this case is that the diagnosis was made at a time when decisive evidence about some of the cardinal features of the syndrome had not yet been obtained. When, however, a biopsy of the testis and the breast tissue were examined microscopically, and when the excretion of gonadotrophic hormone was estimated, the findings corresponded exactly with those described in the two papers on the subject under discussion, and thus it may be stated that the treatment, although achieving all that it purported to achieve, had no influence on the underlying condition.

Although the syndrome as such seems to be well enough established, there are nevertheless a number of questions which have not yet found a satisfactory answer. There is first of all the question of the order of the features within the syndrome. Are they all coordinated manifestations of one hypothetical underlying condition, or is one of them the primary lesion from which the others result? The latter seems to be the case. It is thought that it is the degeneration of the testis that causes the other constant and variable features. However, no specific cause for this primary testicular degeneration has been suggested so far. Carefully taken histories of the thirty odd patients mentioned in the two publications on the subject have failed to reveal a preponderance of any one factor to which the lesion could be attributed. As a matter of fact, many patients do not know anything about the testicular atrophy until it is found at examination. Their complaints generally concern the more conspicuous features, such as gynæcomastia and sterility.

The absence of any definite ætiological features, together with the readiness with which the whole body responds to the testicular lesion, suggests that the syndrome is the effect of intrinsic rather than of extrinsic factors. It seems possible that some constitutional factor sets an early limit to the development of the testicular structures.

If one grants the primacy of the testicular degeneration, the next question is then: Why is one part of the testicular structures singled out, why are the seminiferous tubules so completely degenerated, while the interstitial cells of Leydig are left more or less intact? To attribute this to a selective action of the hypothetical cause is but to confess our ignorance in other terms. However, the fact remains that the Leydig cells are far less involved than the seminiferous tubules. Klinefelter, Reifenstein and Albright in their original contribution stipulated that the syndrome was one "without A-Leydigism", or to translate this monster into the King's English, they stipulated that the syndrome was characterized by a normal state of the Leydig cells. Actually at first they had the suspicion that the Leydig cells might be increased in number, but they satisfied themselves later that the apparent increase was due to the decrease in the other testicular structures. Nelson and Heller, however, were not so sure about the normal state of the Leydig cells. They found, as Klinefelter, Reifenstein and Albright had found, an apparent increase in the number of these cells; but an analysis of the details of their structure led them to believe that the functional activity of the cells was declining. Still, there remains, as also in our case, a discrepancy between the total loss of the seminiferous epithelium and the at least partial survival of the Leydig cells.

It is this state of affairs that makes the explanation of the other features of the syndrome so difficult. If there was evidence of a universal decrease in the production of androgens, the eunuchoidal features of the syndrome and the increased output of gonadotrophic hormone could be easily explained. However, Klinefelter, Reifenstein and Albright, who postulated full function of the Leydig cells, had, in order to arrive at some explanation, to go to the length of assuming the production by the seminiferous tubules of a hypothetical hormone "inhibin". In their opinion the failure of its production on account of the hyalinization of the tubules causes an increase in the output of the follicle-stimulating hormone and some decrease in that of the luteinizing hormone from the pituitary; this accounts for a lower production of androgen from the normal Leydig cells. In Heller and Nelson's opinion there is not sufficient evidence in favour of the existence of this hypothetical "inhibin". As they assume a definite decline in the function of the Leydig cells—that is, a decreased output of androgens—it is not difficult for them to explain the hormonal and eunuchoidal features of the syndrome. To account for the not infrequently observed discrepancy between the amounts of 17-ketosteroids excreted in the urine and the severity of the clinical features, they remind us of the fact that not all that gives the 17-ketosteroids reaction is acutally androgenic. It seems quite feasible that the proportion of androgenic and non-androgenic 17-ketosteroids in the urine may be altered. In the case of a lower androgen production from the Leydig cells, the adrenal cortex may secrete a larger amount of non-androgenic 17-ketosteroids.

The most difficult feature to explain is the gynæcomastia. One point only is certain—that is, that the development of the breasts is not due to œstrone. In all cases in which determinations have been made, no significant increase in œstrone has been found. Furthermore, the histological structure of the breast is different from that found when breast tisue develops under œstrone stimulation. Klinefelter, Reifenstein and Albright put forward the theory that testosterone in the absence of "inhibin" may cause the gynæcomastia; but as the existence of "inhibin" is purely hypothetical, the theory will receive hardly any support from others. Heller and Nelson have also no clear-cut answer to the question why the gynæcomastia develops. They draw attention to a similar condition in functional castrates and in eunuchs, and reiterate an idea that they had advanced on a previous occasion—that is, that some precursor of the 17-ketosteroids formed in the adrenals has mammogenic activity if not counteracted by

the secretion of the Leydig cells. They admit that the nature of this substance is unknown; as a matter of fact, its existence is as hypothetical as that of the "inhibin" of Klinefelter, Reifenstein and Albright.

An additional difficulty lies in the discrepancy between the degree of development of gynæcomastia on the one hand and the eunuchoidal features on the other hand. If both were due to nothing but the lack of androgen, one would expect a parallel development of both conditions. In fact, however, one sees the highest degrees of gynæcomastia usually in the absence of eunuchoidal features, and *vice versa*. To us the following way of reasoning has suggested itself:

First of all, the breasts appear to receive some stimulus to develop from the gonads at puberty, and it does not seem to matter whether from a testis or from an ovary, as some breast development is noticed in both sexes. However, it seems necessary for any later breast development that such a stimulus shall be received, even if it is soon overcome and finally suppressed by the effects of androgens as in all normal males. An observation of two so-called "male pseudo-hermaphrodites" strongly suggests such a mechanism. Both had practically identical features, the only difference being that in the first case the testes were removed at the age of twenty-three years, while in the second case the operation had been performed at the age of about six. In the first case a good development of breasts was easily obtained by œstrone injections, whereas in the second case hardly any result was achieved.

If our idea of the necessity for primary stimulation of the breast by a gonad was correct, then the time of onset of the testicular degeneration would be the factor that would be responsible for the discrepancy in the clinical picture. If the testicular degeneration occurred before puberty, eunuchoidal features would develop to a high degree, but gynæcomastia would not occur for the lack of a primary stimulus. On the other hand, the later the testicular degeneration set in, the less one would expect of eunuchoidal features; but gynæcomastia would develop on account of a lack of suppressive action by androgens. This hypothesis seems to us to have the advantage of not involving the assumption of new, so far unknown, hormones and of giving at least some explanation for the occurrence of gynæcomastia, as well as of the discrepancy between its development and that of the eunuchoidal features.

Practical Applications.

It follows from this discussion that while certain features of the syndrome are not amenable to any kind of treatment, others can be treated with considerable benefit to the patient.

The degeneration of the seminiferous tubules has usually progressed beyond the possibility of repair, and nothing whatsoever could restore them to functional activity. In consequence, such a patient will remain sterile, although he may have satisfactory sexual relations. The condition of the breasts will likewise not respond to any medical treatment, and their surgical removal is indicated.

The administration of testosterone, however, will have a beneficial influence on most of the other features of the syndrome. How far it will correct the general body configuration will depend on the age of the patients. When all the epiphyseal lines are closed, no change can be expected any more. However, the development of the external genital organs, and of hair on the face, in the axilla and in the pubic region, will be greatly enhanced. The voice will break, but most important will be the improvement of the muscular strength and especially the psychological development. This has been clearly shown in our case after a short course of treatment, and has been stressed again and again in the cases reported in the literature. The method of choice in administering testosterone is undoubtedly the implantation of pellets. It is regrettable that such material is not available in this country. We have seen in our case an excellent result from the sublingual administration of methyl testosterone tablets; however, Heller and Nelson have been rather disappointed with their effects. Injections are effective, but cannot be given over an indefinite length of time.

Conclusions.

After this discussion it seems hardly necessary to summarize the points which make the recognition of the syndrome so valuable. It is true that certain features such as the sterility and some characteristics of the body build cannot be cured. The gynæcomastia has to be treated surgically. However, medical treatment will bring to such patients physical fitness and mental altertness which they have not enjoyed before; their lack is often not fully realized, because it is overshadowed by the more obvious embarrassment caused by gynæcomastia.

Summary.

1. Attention is drawn to a new syndrome first described by Klinefelter, Reifenstein and Albright.

2. A description of the constant and of the variable features of the syndrome is given.

3. A case belonging to this syndrome is described.

4. A discussion of the causal and of the formal genesis of the syndrome is presented.

5. The practical applications arising from the recognition of the syndrome are discussed.

Acknowledgement.

The work of one of us (B.R.) has been supported by a grant from the Fletcher fund through Professor P. MacCallum, whose help and advice are gratefully acknowledged.

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Legends to Illustrations.

FIGURE III.—Low-power photomicrograph of testicular biopsy. Hyalinization of practically all seminiferous tubules.

FIGURE IV.—A group of hyalinized tubules under high magnification.

FIGURE V.—One of the few surviving tubules lined by Sertoli cells and some Leydig cells.

FIGURE VI.—A group of Leydig cells between hyalinized tubules.

FIGURES VII and VIII.—Two sections from the breast tissue. Ducts only in dense fibrous tissue. No alveoli developed.

TOXOPLASMIC ENCEPHALOMYELITIS, WITH THE REPORT OF TWO CASES.

By E. GRAEME ROBERTSON, M.D. (Melbourne), F.R.C.P. (London), F.R.A.C.P.,

Melbourne.

TOXOPLASMA is a protozoon parasite of the animal kingdom, with a widespread geographical distribution. It was first recognized in animals independently by Nicolle and Manceaux and by Splendore in 1908.

In 1914 Castellani described parasites which he believed to be toxoplasma in smears of the blood and spleen of a Cingalese who suffered from a fatal illness characterized by fever, anæmia and splenomegaly. However, there was no further advance until Wolf and Cowen[1] in 1937 described the clinical and pathological features of an unusual form of encephalitis in an infant, who died at the age of twenty-eight days. They recognized the presence of an unusual intracellular and extracellular infecting agent, occurring singly or in cyst-like groups. By transmission of infected material from another patient to animals, and by cross-immunity experiments, Wolf, Cowen and Paige[2] subsequently proved the organism to be toxoplasma. The features of the disease were gradually

unfolded in a series of articles by these authors and their associates.[2][7][9][10][11]

Sabin,[2] who had studied the parasite in animals, played an important part in the development of knowledge of the disease. He described two cases of acute encephalitis in older children, assisted in the identification of the parasite and developed laboratory tests for the recognition of the disease.

At a later date Pinkerton and Weinman[4] and Pinkerton and Henderson[5] described toxoplasmic infection of adults. The clinical picture in these cases was one of interstitial pneumonitis, myocarditis and an exanthem simulating that of typhus or spotted fever. Sante[7] studied röntgenograms from two cases described by Pinkerton and Henderson[5] and pointed out that the Röntgen picture was that of any of the atypical or virus pneumonias.

Paige, Cowen and Wolf[17] present incontrovertible evidence that the infection may begin *in utero*, although the maternal infection is symptomless. It seems probable that the reservoir of toxoplasmosis in animals and birds is the source of human infection; but the natural mode of transmission is unknown.

Sabin[2] summarizes the various clinical forms of the disease as follows:

1. Abnormal enlargement of the head *in utero* which is the result of encephalomyelitis in the fœtus.
2. Encephalomyelitis of the newborn (originating *in utero*) which terminates fatally during the first days or weeks of life.
3. Congenital encephalomyelitis giving rise to hydrocephalus or microcephaly, cerebral calcification, chorioretinitis and nervous disturbances such as convulsions ("epilepsy"), spasticity, mental deficiency observed in infancy and early childhood.
4. Atypical encephalitis, exhibiting twitchings of isolated muscle groups, convulsions, disorientation, low-grade fever and pleocytosis, but thus far, without the so-called "signs of meningeal irritation" (nuchal rigidity, Kernig sign, etc.) and without signs pointing to involvement of the cranial nerves.
5. Acute febrile exanthematic disease associated with atypical pneumonia.
6. A mild or inapparent infection betrayed only by the possession of antibodies against toxoplasma or giving birth to an infant with clinically apparent toxoplasmosis.

After reviewing the pathological findings, Sabin concludes that in the fœtus and in early infancy nervous tissue suffers most. In the acquired infection in children the central nervous system may still bear the brunt of the attack. In adults the attack on viscera appears to predominate, although toxoplasma parasites are widely disseminated throughout the body.

Cowen, Wolf and Paige,[9] in the sixth paper of the series, deal with the clinical picture in the congenital and infantile cases (that is, the second and third groups of the above classification). They point out that there is an acute phase, in which the infection is probably active, and a later residual phase. The following are the chief features of these phases which may be recorded in the authors' succinct words.

In the early phase, (1) onset at birth or shortly thereafter; (2) convulsions; (3) hydrocephalus, clinically apparent or demonstrable by pneumencephalography; (4) other inconstant neurologic symptom, such as tremors, twitches, spastic contraction of the extremities and evidence of transverse myelitis; (5) bilateral focal chorioretinitis, almost invariably involving the macula; (6) other ocular signs, such as microphthalmos and ocular palsies; (7) intracerebral calcification, often multiple and bilateral and involving the cerebral cortex and basal ganglia; (8) neonatal jaundice, occasionally lasting many weeks; (9) hepatosplenomegaly, which occasionally may last for many months; (10) interstitial pneumonitis, rare (?) (1 case); (11) xanthochromia, moderate round cell pleocytosis and high protein content of the cerebrospinal fluid, presence of toxoplasma in smears; (12) occasional anæmia and leucopenia; (13) recovery of toxoplasmas from the blood or cerebro-spinal fluid by inoculation of mice and rabbits intracerebrally and intraperitoneally; and (14) demonstration of neutralizing antibodies to toxoplasma in the blood.

In this phase the infant may die within a few days after birth or within the first few months of life. Of the aforementioned features the outstanding clinical findings are the chorioretinitis, the intracerebral calcification, the convulsions and the hydrocephalus.

If the child survives the picture is modified. It is characterized by (1) healed or inactive chorioretinitis; (2) reduced vision; (3) strabismus, nystagmus and microphthalmos; (4) persisting intracerebral calcification; (5) continuance or late appearance of generalized convulsive seizures or *petit mal* attacks; (6) chronic hydrocephalus; (7) retardation of speech development; and (8) mental deficiency, usually mild.

In this paper also the authors discuss laboratory tests for the disease. They have shown that it is possible to recognize the organisms by direct examination of blood and cerebro-spinal fluid, but rarely so. Animal inoculation is sometimes successful. Because of the uncertainty of these methods the authors have used a serological test originated by Sabin and Olitsky, in which the power of the patient's serum to neutralize the action of toxoplasma upon the rabbit's skin is tested. Sabin[6] is endeavouring to elaborate a satisfactory complement-fixation test.

The röntgenographic findings are the subject of the eighth paper of the series by Dyke, Wolf, Cowen, Paige and Caffey.[10] They state that intracerebral calcification was visible in X-ray films of eight of the nine patients studied. In six, multiple, bilateral, more or less rounded areas of lime salt deposits, one to three millimetres in diameter, were found; in two the deposition was unilateral. In three instances there were curvilinear streaks of calcification in the basal ganglia or thalami; this is "the most characteristic but not the commonest feature of the disease". The skull was small in two patients, and large in three patients. There was evidence of increased intracranial pressure in three, and in three the ventricles were shown by gas studies to be large. The lung shadows were abnormal in three cases, and an enlarged heart was demonstrated in one other case, in which pathological examination revealed pneumonitis and myocarditis.

The ocular findings are dealt with by Koch, Wolf, Cowen and Paige.[11]

Sabin and Warren[12] give hope that chemotherapy may be of value in combating the human infection. They have tested a large number of antiprotozoal drugs against toxoplasma. Although capable of killing toxoplasma *in vitro*, none had a therapeutic effect *in vivo*. On the other hand, while sulphapyridine and sulphathiazole had no effect *in vitro*, they were found to have a considerable therapeutic and curative effect in infected mice and rabbits, provided a constant effective level was maintained. Apparently mice failed to elaborate specific immune substance, so that death resulted when the dosage was stopped. On the other hand, rabbits remained well after cessation of drug therapy and were resistant to later reinoculation. These authors suggest that sulphapyridine and sulphathiazole should be given to affected humans and continued for many weeks after apparent clinical recovery. Penicillin has proved ineffective in combating the disease in mice (Augustine, Weinman and McAllister[13]).

Reports of Cases.

The first case to be described is that of a girl, N.D., aged thirteen years, who was referred from Tasmania by Dr. Bruce Hamilton, Dr. R. Whishaw and Dr. O. T. Kyle (Figure I). She was born in Tasmania and was the eldest of five children, the others being healthy. The mother was intelligent; the father stuttered badly, and had reached the fourth grade at school when he was twelve years of age. He was a farmer. The home conditions were clean and free from vermin. The mother milked cows and occasionally dressed poultry. No domestic pets were kept, and rabbit flesh was not eaten. The pregnancy was normal. The premature labour was an easy one and lasted for twenty-four hours, terminating before the arrival of the doctor in the birth of a baby, weighing five pounds and of normal colour.

The infant sucked readily. Teeth appeared normally, and she walked at ten months. At an early age her parents noted that the right eye was smaller than the left. When she was two years of age, she was able to compose sentences of small words, but her speech remained difficult to understand and her vocabulary did not expand normally. She

was dull at school and never learned to read or write more than her own name. Because her eyesight was thought to be bad, when she was seven she was taken to Dr. Bruce Hamilton. During her twelfth and thirteenth years she had eight convulsive seizures, all except three occurring as she was falling asleep. When her parents rushed to her, she was found to be cyanosed, and her left arm and leg twitched for some seconds. She recovered consciousness after some five minutes, and then fell asleep a few minutes later. The character of the attacks changed when she was twelve years of age. She complained of a peculiar feeling in her left arm and hand. She then screamed that she had "an awful headache", and as she shouted her left arm became rigidly elevated and her head turned to the left. She then lost consciousness and lay inert for about ten minutes. Two similar attacks followed at intervals, and in between these attacks she frequently complained of "pins and needles" and a dead feeling in her left arm and hand. Since the first convulsive seizure she had suffered from severe frontal headache, which occurred at intervals of one or two weeks. The pain lasted for one to one and a half hours, and was likely to occur after she had been running about in the hot sun or after travelling. She preferred to lie down when she had a headache, but did not complain of feeling ill. Previously a happy child, she had become miserable, morose and disinterested in the last six months.

FIGURE I.
Photograph of first patient.

Menstruation commenced when she was twelve years of age. She was well developed physically, although her head looked small, having a circumference of 21 inches. She was unable to name letters, even though she could write her name. Although endeavouring to cooperate, she was unable to comprehend any but the simplest requests. She met most situations with an inane grin, which was excessively broad and unduly persistent. Her emotions were ill-controlled, both laughter and tears being easily provoked and unrestrained. Her speech was staccato and explosive, the syllables being poorly separated.

The right palpebral fissure was narrow and the right eye was smaller than the left. The horizontal diameter of the right cornea was 0·75 centimetre and that of the left was 1·1 centimetres. The right pupil was small and failed to react to light thrown in either eye and to accommodation; the left reacted to direct illumination, to light thrown on the right eye and to convergence. Remnants of pupillary membrane could be readily seen within the fixed right pupil, arising from the collarette of the iris and adherent to the capsule of the lens. She was able only to distinguish light from dark with her right eye. The visual acuity of the left eye was $^{6}/_{12}$ (Snellen). Accurate testing of the visual fields was impossible, but confrontation tests and perimetry revealed a slight generalized contraction of the field of the left eye. Upward rotation of the eyes was defective, other movements being full. No other abnormalities were detected in the cranial nerves. The grip of the left hand was weak. Movements of her arms and legs were clumsy and alternating, and fine movements were slowly and irregularly performed. No abnormality of muscular tone was detectable and no muscular wasting was present.

The deep reflexes were all brisk, especially on the left side. The superficial abdominal reflexes were present; the plantar responses were flexor in type. Sensation appeared to be normal. General examination revealed no abnormality.

X-ray examination of the skull (Figure II, (*a*) and (*b*)) revealed widely scattered areas of calcification, chiefly in the lower and outer parts of the parietal lobes and more pronounced on the right side. One small round mass was seen in the right frontal lobe. Symmetrical comma-shaped deposits were seen in the region of the caudate nuclei. The bones were thick, and well-marked digital impressions were seen in them. The cerebro-spinal fluid was under an initial pressure of 110 millimetres. The pressure responded normally to jugular compression. The fluid was clear and colourless. No cells were seen in three cubic millimetres. The total protein content was 80 milligrammes per 100 millilitres. There was no increase in globulin content. The colloidal gold curve was normal ("000000000"). The Wassermann test failed to produce a reaction in the blood and the cerebro-spinal fluid.

At encephalographic examination the *cisterna magna*, the fourth ventricle and lower part of the aqueduct of Sylvius filled with gas and appeared normal. The shadow of the aqueduct, however, terminated abruptly, the upper part failing to fill. No gas reached the third or lateral ventricles. When more gas was injected, it passed into the interpeduncular, chiasmatic and ambient cisterns, then into the cerebral sulci, all of which appeared normal.

Treatment with "Dilantin" and phenobarbital has abolished the epileptic manifestations, and the patient has become once more happy and docile in disposition.

That the diagnosis is readily made once the condition is known is illustrated by a second case.

J.J. was first examined by Dr. L. P. Wait at the Children's Hospital, Melbourne, at the age of five weeks, having been referred from the Women's Hospital because she was thought to be hydrocephalic. The pregnancy had proceeded to full term, although *placenta prævia* had caused a hæmorrhage at seven months. Labour was apparently normal, but a soft prominence remained in the occipital region for ten days after the child's birth. The circumference of the head increased at the rate of a quarter of an inch a day for four days, and then abnormal expansion ceased. When she was examined at this time the baby was thought to be lethargic. There was no evidence of hydrocephalus, the fontanelles appearing normal. The left eye was noticed to be smaller than the right, and the media on this side were opaque. Dr. Nancy Lewis reported that the left eye was small. The cornea was clouded, and no red reflex could be obtained. The pupil was irregular, and posterior synechiæ were present. On the right side chorioiditis was evident, and fine posterior synechiæ were observed. X-ray films of the skull revealed two faint crescentic areas of calcification, apparently in the region of the basal ganglia.

At the age of thirteen months the child was brought back to hospital, because her mother feared that her eyesight was defective. The cephalic circumference was now 17·5 inches. The condition of the eyes was apparently unaltered. The right pupil reacted to direct but not to consensual light. The left pupil was fixed. No abnormal neurological signs were detected, apart from evidence of delayed mental development. The calcification seen in the X-ray films appeared more dense, although of the same distribution as before.

Comment.

The close correspondence of the signs and symptoms with the clinical picture described by Cowen, Wolf and Paige leaves little doubt that the patients had suffered infection with the protozoon toxoplasma in intrauterine life, and had survived the infection. However, it is possible that other infections may lead to a similar residual condition. In order to make certain of the diagnosis, fresh and dried serum was sent for testing to Dr. Wolf, but proved unsatisfactory. Sabin[3] states that the antibodies are labile. However, even without this confirmation, the cases seem worthy of report in order to direct attention to the occurrence of the disease in this country. Laboratory confirmation would be of great value in a number of other cases which may also be examples of this disease, although the manifestations are less typical.

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Reports of Cases.

NESIDIOBLASTOMA: REPORT OF TWO CASES RESPONDING TO SURGICAL REMOVAL.

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NESIDIOBLASTOMA, a word coined by Laidlaw (1938), is the term now applied to infiltrating tumours of the islets of Langerhans which consistently produce the syndrome known as "organic hyperinsulinism". Harris in 1924 described the symptoms of spontaneous hypoglycæmia in a non-diabetic individual, and their regression when a diet low in carbohydrate was taken. Common to all cases is a history of "spells" of loss of memory and disorientation, sometimes of epileptiform convulsions, associated with a fall of the blood sugar level to below 50 or 40 milligrammes *per centum*. Not all instances of organic hyperinsulinism arise from intrapancreatic causes, and clinical hypoglycæmia may arise from disorder of the adrenal, thyreoid, pituitary or liver. Our present concern, however, is with neoplasia of one or more of the islets of Langerhans, of which condition the first clinical description was recorded by Wilder and his associates in 1927. The first successful surgical cure was reported by Howland and associates two years later (1929). By 1935 Whipple and Frantz were able to collect records of 28 cases, including eight of their own. According to Meyer and others writing in 1941, this number had grown to 171 cases confirmed by operation. Unfortunately in 31 of these cases malignant changes were found on histological examination. In 1942 the number of cases reported was 134 (Whipple).

The criteria for diagnosis of this striking clinical syndrome and the indications for surgical exploration are nowadays universally accepted. Hitherto, however, no case reports have appeared in Australian medical literature. The following descriptions concern two female patients admitted to the Royal Prince Alfred Hospital, Sydney, in the period from 1942 to 1944.

CASE I. (T.M.G.)

Clinical Record.

A female patient, aged thirty-eight years, was admitted to hospital first in 1937, for the investigation of episodes of coma. On this occasion the provisional diagnosis was cerebral thrombosis. She was stuporose, there was rigidity of the right arm and leg, and the plantar response was extensor in type on both sides. The blood sugar level during stupor was 43 milligrammes *per centum*. She regained consciousness dramatically when given milk and glucose by stomach tube. A sugar tolerance test was performed, the results of which are set out in Table I. Full investigations of all systems were carried out, but with negative findings, except in regard to the blood sugar curve. After a stay of six weeks in hospital she was discharged with a diagnosis of spontaneous hypoglycæmia due to pancreatic dysfunction.

After her discharge from hospital, however, she was seldom free from symptoms, especially when about her daily duties, and she was eventually readmitted in 1941 on account of prolonged hypoglycæmic coma. At this time the gastro-intestinal features of the attacks, in particular obstinate vomiting, were more prominent than the nervous phenomena. She remained in hospital for one week, and during this week she appeared to have developed a permanent tremor.

In 1942 she complained that, despite a liberal intake of carbohydrate, she was having frequent peculiar attacks—up to ten each day—with occasional episodes of actual unconsciousness. The minor "turns", which were precipitated by fasting or by exertion, were associated with vomiting, tremulousness and frequently hunger. Her weight at this time was 130 pounds. Her facies was not unlike that presented by some patients suffering from Parkinsonism—it had a rather mask-like appearance—and tremor of the hands was present.

As a diagnosis of pancreatic hyperinsulinism was now almost certain, the abdomen was opened on December 8, 1942, by Dr. B. T. Edye. An upper abdominal transverse incision was employed, as this affords the best approach to the whole of the pancreas. A tumour arising from the body of the pancreas near the middle line was exposed. It was partly solid and partly cystic, rounded in shape, and approximately eight centimetres in diameter. There was also a large chronic ulcer on the posterior wall of the duodenum, penetrating the head of the pancreas, and forming an indurated mass five centimetres in diameter to which the gall-bladder was also adherent. The pancreatic tumour was excised. It arose out of the substance of the body of the pancreas, portion of which spread on to the attached area of the tumour. The defect in the pancreas was oversewn. The adjacent pancreatic tissue was firm, but no search for other adenomata was made. Posterior gastro-jejunostomy was performed. A drainage tube from the oversewn area of the pancreas was brought through a stab wound above the main incision. Glucose solution was given intravenously during and after the operation (see Table II) and insulin was necessary to control the resulting hyperglycæmia. A few days after the operation pancreatic secretion began to escape freely from the drainage tube. This secretion was removed by suction and the amount gradually lessened until the secretion ceased altogether. Obviously one or more small pancreatic ducts had been injured during the separation of the tumour. The gastro-jejunostomy functioned satisfactorily.

For twelve months after this operation the patient remained well, except for a peculiar attitude towards her everyday affairs and a strange vacuity. However, on March 7, 1944, she was readmitted to hospital in coma. On the assumption that another tumour was present, the abdomen was opened again. The same surgical approach was employed as at the first operation. After some filmy adhesions had been separated the pancreas was exposed and examined from various aspects. The body and tail of the organ were viewed above the stomach, and the anterior aspect of the head was also seen. The posterior aspect of the head was examined by dividing the peritoneum lateral to the second part of the duodenum, and turning both the duodenum and the head of the pancreas over towards the left. Up to this point no tumour was detected. The tail was again examined, and near its tip

adjacent to the spleen a small mass was felt. It was decided to resect the tail and portion of the body of the pancreas, as it would have been difficult to enucleate the mass. The body of the pancreas was isolated at a point where it was narrow, but an attempt to separate the tail from the splenic vessels proved impossible, because of the close relationship of the structures and the persistent hæmorrhage. It became clear that the best way to overcome the difficulty was to remove the spleen also. The body of the pancreas was divided and the proximal end sutured with silk. The splenic vessels were next ligated and divided. The distal portion of the pancreas, together with the tumour, was separated from its surroundings,

FIGURE I.—Tumour 1A (natural size).

and the removal of the spleen was completed from the lateral aspect after the gastro-splenic omentum and associated structures had been divided. Before the abdomen was closed, a small drainage tube was brought through the site of the original stab wound. During the operation a 5% solution of dextrose was given intravenously, followed by blood transfusion. There was no drainage from the tube, which was removed in a few days. The wound again healed well, and recovery from the operation was uneventful. Up to the time when this paper was written (March, 1945) the patient has remained well.

Pathological Report.

Tumour IA.

The specimen submitted for pathological study was a cyst, measuring 9·2 centimetres by 7·2 centimetres by 5·5 centimetres. When opened it was found to comprise two main loculi with thin fibrous walls, each containing pale, semi-solid gelatinous material. The wall common to the two loculi was composed of a thick mass of pale, solid, neoplastic tissue of homogeneous appearance, and measuring approximately 3·3 centimetres by 2·0 centimetres in its widest part and 2·0 centimetres in thickness. It projected irregularly into each loculus to a height in some places of 1·0 centimetre above the general level. Further somewhat ragged fragments of tumour tissue of similar appearance were attached to the inner wall of the smaller loculus, together with some blood clot. The larger loculus had a thinner wall and contained no outlying tumour masses. However, some fibrous strands were stretched accross its inner surface.

Microscopic examination showed the tumour to be cellular; it was composed of small cells, mostly polygonal in shape, but some tending to a cuboidal form, with scanty eosinophilic cytoplasm and oval nuclei containing an open chromatin network and a single nucleolus. The cellular pattern was somewhat indefinite. In some areas there was a slight tendency to a branching papillary structure, superimposed in which were small rudimentary alveoli, incomplete tubules and short strips of tumour cells. However, the tumour also showed such rudimentary tubules and cell strips without any papillary structure, intermingled with a less differentiated pattern; in many places the tumour cells abutted directly upon small blood capillary channels, sometimes with, but often without, any intervening visible endothelium. In other areas was a good deal of scattered, patchy, hyaline degeneration. The hyaline material, which took on connective tissue stains, had been deposited in the interstitial tissue, often separating strips of tumour cells. In many places it could be seen that it had been deposited beneath the endothelium of capillary blood vessels, so that the vessel was reduced to a narrow channel seemingly scarcely wide enough to afford passage to an erythrocyte, and lying in the centre of a wide collar of hyaline material. No intracellular hyaline droplets could be made out. Mitotic figures were scanty. A somewhat hyaline fibrous capsule surrounded the tumour.

Tumour IB.

The second specimen received from Case 1 (tumour IB) comprised portion of the tail of the pancreas, 6·5 centimetres in length, to which was attached the spleen, which measured 7·5 centimetres by 6·5 centimetres by 2·5 centi-

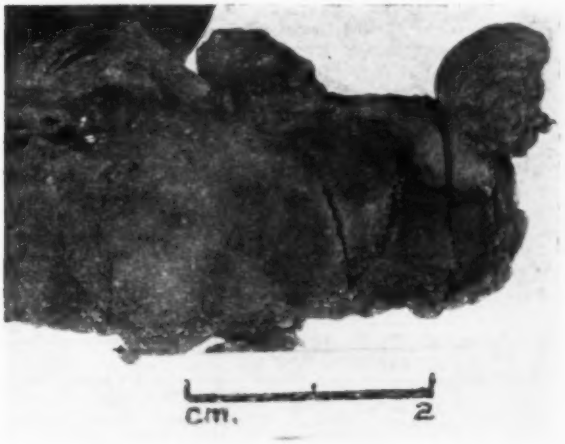

FIGURE III.—Tumour IB.

metres. The inner extremity of the portion of pancreas was firmer on palpation than the lateral or splenic extremity. It was divided longitudinally, to expose at its inner end a neoplasm measuring 3·0 centimetres by 2·0 centimetres by 2·0 centimetres, composed of three adjacent, partly-merged, rounded lobules. The most laterally situated of those lobules was pale yellowish, homogeneous, and slightly translucent in appearance. The medial lobule had a background of pale tissue of similar appearance, but was mottled with small reddish areas, while the innermost lobule was of a moderately uniform, brownish-red colour and had a deeply hæmorrhagic periphery. Bounding the whole tumour was what seemed to be a fibrous capsule. The pancreatic substance lateral to the neoplasm was somewhat firmer than normal and contained many prominent small blood vessels. No normal pancreatic tissue was present beyond the tumour at the medial end.

TABLE I.
Case I: Sugar Tolerance Curves.

Time of Test.	1937.		Before First Operation. November 11, 1942.		After Second Operation.			
					April 27, 1944.		August 2, 1944.	
	Blood Sugar. (Milligrammes *per Centum.*)	Urine.	Blood Sugar. (Milligrammes *per Centum.*)	Urine.	Blood Sugar. (Milligrammes *per Centum.*)	Urine.	Blood Sugar. (Milligrammes *per Centum.*)	Urine.
Patient fasting	45	—	43	—	115	—	70	No sugar, no acetone.
Half an hour after 50 grammes of glucose	150	—	150	—	159	—	159	Sugar present, no acetone.
One hour after 50 grammes of glucose	190	—	186	—	195	Sugar present, no acetone.	260	"
One and a half hours after 50 grammes of glucose	180	—	177	—	177	—	290	
Two hours after 50 grammes of glucose	172	—	88	—	177	—	177	Much sugar present, no acetone.

On microscopic examination this tumour was seen to be slightly more cellular than tumour IA. The cells were small with eosinophilic cytoplasm, and had oval nuclei of similar structure to those in tumour IA. In this second tumour (the recurrence), however, the cellular pattern was much more definite. In most of the tumour were seen circlets, long strips, tubules and larger tumour-lined spaces, made up of a single layer of cuboidal cells lining a cavity. Many of these small spaces were blood channels and contained red blood cells. No endothelial lining could be made out as separating the tumour cells from the lumen. Some of the spaces contained what appeared to be coagulated albuminous fluid. In some places the multicystic

TABLE II.
Other Findings in Case I.

Period.	Date.	Blood Sugar. Milligrammes *per Centum.*)	Remarks.
First admission to hospital.	2.11.42	43	Fasting.
	24.11.42	53	Hypoglycæmic symptoms.
	4.12.42	53	Hypoglycæmic symptoms.
	8.12.42 (during first operation)	177 168 159	Glucose being administered intravenously.
	11.12.42	159 195	Glucose being administered intravenously.
	14.12.42 to 30.12.42	97–168	Daily values varied between these limits.
Second admission to hospital.	7.3.44	25	Patient unconscious.
	9.3.44	35	
	7.4.44	437	Post-operative; patient having glucose intravenously.
	8.4.44	290	Patient having glucose.
	11.4.44	220 310	
	18.4.44	106	Fasting.

appearance was so pronounced that the tumour cells appeared as relatively attenuated twigs and strands partially separating large spaces usually containing blood. Large areas of hyaline change were conspicuous. In this tumour also, as in tumour IA, the hyaline material was deposited apparently in the interstitial tissue, and very often beneath the endothelium of vessels. In places it was so dense that the tissue was composed of angular hyaline masses separated by capillary blood vessels and showing only a few degenerating tumour cells, apparently compressed between the hyaline masses and the walls of the vessels. In further areas was found a structure duplicating more closely a normal islet. Here the cells had pale, clear cytoplasm and an irregular, ill-defined branching outline, and were formed into a loose, uniformly cellular tissue, with small circular intercellular spaces, some apparently empty, others containing red blood cells.

An ill-defined fibrous capsule surrounded the tumour, outside which the adjacent pancreatic lobules were considerably compressed. In these lobules islets of Langerhans, both large and small, were abundant, and gave the impression of being somewhat more numerous than usual. Evidence of infiltration of the fibrous capsule by the tumour was present in several places, indicating that it had definite invasive properties.

CASE II. (J.K.M.)

Clinical Record.

Mrs. C.A., aged fifty-seven years, was referred for admission to the Royal Prince Alfred Hospital, where she had once trained as a nurse, by Dr. Richmond Jeremy, of Sydney. Apart from an attack of scarlet fever, and a tonsillectomy, her previous medical history had been uneventful. One sister suffers from *diabetes mellitus*. No other relations are known to be so affected. In six months prior to her admission to hospital she had experienced "dizzy turns" in the early morning. Three months before, the first attack of disorientation, lasting for three or four hours, appeared in the early morning. A subsequent attack, lasting for six hours, was observed by Dr. Jeremy, who writes as follows: "She was conscious, but vague, rambling and repetitive in her speech. She was neither flushed, nor pale and sweating as her daughter (a nurse) had reported her to be in a previous attack." She recovered spontaneously, and was subsequently clear, concise and intelligent, but with complete amnesia concerning the period of her attack. There were no nervous sequelæ in the form of somnolence, paresis, sensory disturbances or emotionalism. Between attacks she felt completely normal, and entirely devoid of any symptoms referable to her cardio-vascular or nervous systems.

Physical examination gave completely negative findings. An unusually composed and intelligent patient, she displayed no abnormalities of manner or speech and possessed a normal, healthy appearance. There were no scars on the head or tongue to mark past epileptiform seizures, no evidence of arterial degeneration or hypertension, no evidence in the fundi of a raised intracranial pressure, nor of focal damage to the central nervous system. She was devoid of any stigmata of psychoneurotic illness. The liver and spleen were impalpable, and no tumour was discernible in the epigastrium.

In this instance the history and the completely negative results of physical examination led to the suspicion of hypoglycæmia, which was readily confirmed by a period of twenty-four hours' starvation. This resulted in an attack indistinguishable from that described by Dr. Jeremy. The attack was relieved by the administration of one ounce of 50% glucose syrup. After recovery (March 20, 1944) the blood sugar level was still at 60 milligrammes *per centum*. A glucose tolerance test (Maclean) three days

later put the diagnosis beyond all doubt, the blood sugar level never having risen above 43 milligrammes *per centum* during the whole test. During the test the patient was mentally confused. At this point the patient was placed on a diet rich in fat and low in carbohydrate; the diet was of 2,000 Calories, composed as follows: protein 73 grammes, fat 148 grammes, carbohydrate 96 grammes. The institution of this diet was an attempt to repress her secretion of insulin. An extensive series of investigations was undertaken to elucidate the cause of the hyperinsulinism, and to inquire into the function of organs concerned in carbohydrate metabolism. The following investigations provided normal results: a blood count; the Wassermann and Kline tests; the estimation of the prothrombin index, the blood chloride content, the blood urea level, the blood cholesterol content, and the basal metabolic rate; the hippuric acid test of liver function; an electrocardiogram (between and during attacks); a cholecystogram; a radiograph of heart and lungs. No evidence was forthcoming in regard to any physical change in the hypophysis as a result of examination of the cranial nerves, including the optic fundi and the fields of vision. The *sella turcica* was normal in appearance. No tumour was palpable in the region of the pancreas or adrenal, although pneumography and investigation of blood steroids were not carried out. The excretion of chlorides over a twenty-four hour period was estimated before operation, when the patient was having a fixed salt-free diet. During the first twenty-four hour period the chlorides excreted amounted to 3·5 grammes expressed as sodium chloride. During the second twenty-four hour period the equivalent of 3·0 grammes was excreted. It will be observed that subsequent to operation this amount excreted rose to 5·7 grammes in twenty-four hours. This appears to be the inverse of what happens in *diabetes mellitus* before and after stabilization.

Many estimations of the blood sugar content were made, and the results appear in Tables III and IV. Long-term sugar tolerance tests and the plotting of blood sugar curves were omitted because of manpower reasons. The patient's attacks lessened while she was in hospital, probably because she rested in bed most of the time. Occasional hypoglycæmic episodes of a mild type were encountered. The high fat diet was not tolerated well, and it is difficult to say whether it was a success. Later a trial was made of œstrogen therapy, as this is stated to raise the blood sugar level and to have an anti-insulin effect. One milligramme of stilbœstrol was administered by mouth three times a day without benefit. She left hospital for a brief period, and tried to manage the high fat diet. One or two severe attacks induced her to return and complete the relevant investigations. As there now seemed every likelihood that an islet tumour was present, Dr. B. T. Edye explored her pancreas surgically. Operation was performed on May 30, 1944. As in Case I, an upper transvere abdominal incision was used. The pancreas was examined from all aspects, and finally after a long search a small plum-coloured adenoma 1·0 centimetre in diameter, hard, rounded and circumscribed, was detected presenting on the anterior surface of the tail 2·0 centimetres from its extremity. The tail was separated with difficulty from the splenic vein which grooved its deep surface, and was then divided 2·0 centimetres proximal to the adenoma. The proximal cut surface was sutured with silk. The pancreas was carefully examined again to exclude other adenomata. A small drainage tube was brought from the vicinity of the pancreatic resection through a stab wound above the main incision. Glucose solution was given intravenously during the operation. Recovery was satisfactory.

Pathological Report.

The specimens submitted from Case II consisted of a piece of pancreatic tissue, measuring 3·3 centimetres in length, and 1·7 centimetres at its widest part. From the external aspect it appeared for the most part normal, but a small, deep, reddish-brown, smooth swelling was present on its surface towards one end. The specimen was divided longitudinally, through the centre of the swelling (Figure VI). The cut surface of the tumour had a smooth homogeneous appearance and a deep red colour. The tumour was somewhat reniform, measuring approximately 1·1 centimetres by 0·6 centimetre by 0·5 centimetre, with a rather definite "hilum". The convexity of the tumour projected from the surface of the pancreas. The concavity or "hilum" showed no definite demarcation from the adjacent somewhat fibrous pancreatic tissue, even under magnification. In fact, several small outlying masses of deep red tumour tissue could be easily made out with the dissecting microscope in the fibrous tissue in this situation. The bulk of the specimen was composed of pancreatic lobules, which appeared normal both to the naked eye and under low magnification.

On microscopic examination the tumour was found to present two main types of cellular pattern, one resembling pancreatic duct tissue, the other more closely resembling true islet tissue. In the first type of pattern there was an arrangement of small groups of tumour cells embedded in a fibrovascular stroma. The cells were slightly larger than those of tumours IA and IB, but they had oval nuclei with open mesh chromatin and a single nucleolus, as did the cells of the former tumours. They tended to be columnar in form, with eosinophilic cytoplasm, and were orientated in rows of strips of moderate length, resting on collagenous

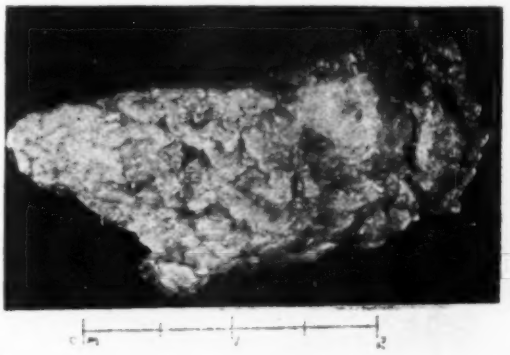

FIGURE VI.—Tumour II.

connective tissue, and projecting directly into one side of a small elongated cavity containing blood, the other side of the vascular space being covered with endothelium resting directly upon connective tissue (Figure VII). In some places these strips of cells were somewhat heaped up, forming two or three irregular layers, the more basally situated cells also being elongated, although somewhat polygonal in form. In other places there was an attempt at tubule formation. In others again the cell groups lay in the connective tissue without any relation to a vascular space. The cells of these groups tended still to be elongated and prismatic from mutual compression.

The other type of cellular pattern, also present throughout large areas of the tumour, was much less definite. Although still divided up into small areas by fibrous tissue septa, the tumour cells were much less regular in appearance. The cell cytoplasm was here clear and the cell outline indefinite, adjacent cells forming a loose meshwork enclosing many small circular spaces, some of which had apparently contained clear fluid while others contained blood. The appearance in these areas (Figure VIII) was much more reminiscent of islet tissue than of ducts, and closely resembled certain areas of tumour IB.

In the portion of pancreas adjacent to the tumour, which appeared normal to the naked eye, there was a great apparent increase in the number of islets (Figure IX). Very many islets were here visible, at times as many as 15 in one low power field. In many cases these islets were very small, consisting of a small group of four to eight pale cells lying among the darker-staining exocrine cells; but all variations existed up to islets at least twice as large as those usually seen.

Rounded masses of neoplastic cells could be seen invading the fibrous tissue at the hilum of the tumour and penetrating among the adjacent pancreatic lobules, indicating that the tumour could not be considered to be benign.

DISCUSSION.

Here we have a clearly defined clinical syndrome, which in its dramatic and unusual guise should be widely recognized. Surgical treatment is eminently satisfactory in the absence of advanced malignant change, corresponding to the success attending ablation of a parathyreoid tumour in *osteitis fibrosa cystica generalisata*. No other treatment, dietetic or medicinal, controls the hypoglycæmic attacks in a classical example of the disease, and such failure has a distinct diagnostic value. Frequent carbohydrate feedings and a diet relatively rich in fat are of more value for sufferers from functional hyperinsulinism. This rearrangement of diet may even exaggerate the number and severity of the attacks, by stimulating a higher total production of insulin, and further inhibiting hepatic glycogenolysis. This inhibition takes place in any case, even when low carbohydrate feedings are employed.

TABLE III.

Case II: Glucose Tolerance Curves.

Period of Test.[1]	March 23, 1944. Before Operation: Blood Sugar. (Milligrammes *per Centum*.)	June 30, 1944. After Operation: Blood Sugar. (Milligrammes *per Centum*.)
Patient fasting	25	106
Half an hour after 50 grammes of glucose	35	115
One hour after 50 grammes of glucose	43	168
One and a half hours after 50 grammes of glucose	43	159
Two hours after 50 grammes of glucose	35	115
Half an hour after 25 grammes of glucose (administered therapeutically)	150	—

[1] The patient was confused and stuporose throughout the test; the urine was free from sugar and acetone throughout.

TABLE IV.

Case II: Blood Sugar Levels.

Date.	Blood Sugar. (Milligrammes *per Centum*.)	Remarks.
20.3.44	60	1 p.m.
24.3.44	79	
3.5.44	35	Patient unconscious.
18.5.44	53	Patient unconscious.
25.5.44	106	After breakfast.
29.5.44	115	After breakfast.
30.5.44	88	Preoperative.
	177	Patient having glucose intravenously.
	300	
	241	
31.5.44	230	Patient having glucose intravenously.
3.6.44	150	
7.6.44	88	Patient fasting.
16.6.44	106	Patient fasting.
20.6.44	97	Patient fasting.
23.6.44	88	Patient fasting.
27.6.44	106	Patient fasting.

Deliberate precipitation of hypoglycæmic attacks by starvation periods is a simple method of confirmation, besides providing the opportunity of blood sugar study before the number of seizures is reduced. The method is probably safe if it is employed in a hospital with facilities for intravenous therapy on hand.

The clinical diagnosis must be made from simple vagovasal attacks, *petit mal* or *grand mal*, hysterical fugue states, intracerebral disease (whether arteriosclerotic, posttraumatic or neoplastic—for example, "ball valve" tumours of the third ventricle), hypertensive encephalopathy, intoxications (for example, lead, alcohol), meningitis, psychosis, internal hæmorrhage, and other conditions. The history of sudden behaviour changes or irrationality, especially in the early morning or before meals and in the absence of headache, and of change in pulse rate, blood pressure, fundi *et cetera*, is well known to those who deal with diabetics on a high insulin intake.

During the attack the patient may sweat, and exhibit pallor, tachycardia, tremors, aphasia, irascibility, disorientation or acute behaviour disorders. On the other hand, somatic signs may be wanting.

These developments occur equally in good health and in the complete absence of other fixed physical or psychic disturbance. When recovery follows the administration of an adequate amount of glucose, the diagnosis is almost certain and should lead inevitably to blood sugar studies.

An important phase of the treatment consists in an adequate pursuit of the patient's history after operation, in view of the frequency of malignant degeneration or the occasional occurrence of multiple tumours. This is amply demonstrated by Case I.

The blood sugar levels at various times in Case I and the results of three glucose tolerance tests have been listed in Tables I and II. It will be noted that hypoglycæmic attacks occurred when the blood sugar level fell below 60 milligrammes *per centum*.

The glucose tolerance curve before the first operation shows normal figures except for the low fasting level. This suggests that the glucose was normally absorbed and that the response of the islet tissue to the demand for insulin was apparently normal. The abnormality in this patient's carbohydrate metabolism could not be determined over the period of two hours during which the test was made—it occurred later. The islet tissue failed to cease pouring insulin into the blood stream after the exciting stimulus—that is, the rising blood sugar level—ceased to act; insulin continued to be produced after the blood sugar level had fallen and hypoglycæmia was the result.

The values obtained after the second operation suggest that at the time of these examinations the islets in the remaining pancreatic tissue were not producing quite enough insulin to cope with 50 grammes of glucose; the blood sugar level rose above the renal threshold and sugar appeared in the urine. As the patient showed no evidence of acidosis, and as the blood sugar level was falling at two hours, the insulin deficiency seemed to be slight.

In Case II the sugar tolerance curve and the frequent attacks of hypoglycæmia suggest a continuous overproduction of insulin which did not need the stimulus of a rising blood sugar level for its initiation.

An attempt was made in this case to extract insulin from the tumour. Immediately after the tumour was removed part of it was ground up with sterile sand and extracted with saline solution and injected into a rabbit. No alteration in the blood sugar level of the rabbit occurred.

The post-operative sugar tolerance curve is normal.

Reported examples of nesidioblastoma have differed widely in naked-eye appearance. The tumours may be cystic, solid, or of mixed cystic and solid types. The solid areas usually appear moderately homogeneous, but they too may show variations in colour and consistency. Tumour IA of this series was of most unusual nature. It was a large bilocular thin-walled cyst, the neoplastic tissue occupying the relatively small central zone common to the two loculi. This neoplastic area was pale, solid and somewhat friable. However, tumour IB (the recurrence) was entirely solid, firmer in consistency and with considerable variations in the colour of the cut surface owing to local differences in the amount of contained blood. The tumour in Case II was much smaller than either tumour in Case I, and was of homogeneous structure and a deep uniform plum colour.

The microscopic patterns seen in nesidioblastomata are in part explicable on the basis of normal developmental potentialities. Grauer, in 1926, showed that the pancreatic duct epithelium was totipotential, giving rise to acini and islets as well as to ducts, and that this potentiality was retained throughout life. In the normal pancreas also there is continuity between islets and rudimentary and inconspicuous ductules. Therefore the appearance in islet cell tumours of structures resembling pancreatic ducts is not surprising.

In the present series appearances reminiscent of islet tissue and of ducts were conspicuous. In many areas in all three tumours there was a loose network of cells with a rich intervening network of capillaries, as is present in the normal islet. In other places in all the three tumours were found short strips of columnar or cuboidal cells

bounding the capillary channels; this finding also is reminiscent of the normal.

In both tumours in Case I, but especially in tumour IB, long strips, rudimentary tubules and small cystic spaces, lined by a regular cuboidal epithelium, produced striking appearances over large areas, and in all probability represented an attempt at duct formation. In tumour II a further caricature of the normal was present in the series of heaped-up strips of tall cells which lined one side only of small vascular spaces.

Fibrosis, hyaline degeneration and calcification, all processes commonly seen in the non-neoplastic islet, are common also in nesidioblastomata. Purely fibrotic areas were inconspicuous in the three tumours in the present series; but large areas of hyaline degeneration were present in both specimens in Case I. The hyaline change represented a change in the connective tissue, and no evidence was obtainable for the simultaneous occurrence of intracellular hyaline degeneration. No calcified areas were noted in any of the tumours.

Two of the three tumours were unusually large. Nesidioblastomata are commonly small, often very small, and the fact that they may not cause obvious clinical symptoms during life makes any estimate of their frequency difficult, as this fact, together with their small size, may cause them to be readily overlooked at operation or autopsy unless the pancreas is examined with unusual care.

In some cases of hyperinsulinism no definite tumour as such is present, but rather a diffuse hypertrophy of islet tissue. It is in cases of this type that partial or subtotal pancreatectomy has given good results. Various gradations are met with between cases associated with a discrete isolated tumour and those in which diffuse islet hyperplasia only is present. In both the present two cases (tumours IB and II) islets of Langerhans were prominent in the apparently normal pancreatic tissue adjacent to the tumours, and although no count of the number of islets per unit volume of pancreas was attempted, the impression was gained that there was a degree of diffuse islet hyperplasia present as well as a definite neoplastic mass.

Many reported examples of nesidioblastomata have been considered malignant after histological study; but Hanno and Banks in their review of this subject suggest that the microscopic appearance may be somewhat deceptive and lead to an unnecessarily gloomy verdict. Frank islet cell carcinoma with metastasis is rare, and these workers considered that if malignant disease is present it is mostly of relatively low grade and likely to cause local recurrence rather than frank metastasis. This point was of importance in both subjects of the present report, as in Case I the tumour recurred and in Case II there was evidence of local invasion of adjacent fibrous tissue. The outlook for these patients, if this conception of the invasive potentialities of nesidioblastomata is correct, may be somewhat better than we at one time thought.

SUMMARY.

Two cases of islet cell tumour (nesidioblastoma) of the pancreas, responding to surgical removal, are reported.

The first patient was a female, aged thirty-eight years, with a history of hypoglycæmic attacks of five years' duration, from whom a large cystic islet cell tumour was removed at operation. Hypoglycæmic symptoms recurred after twelve months of good health, and at a second operation a solid recurrent tumour was excised, with restoration of good health.

The second patient was a female, aged fifty-seven years, with a history of hypoglycæmic attacks of six months' duration, from whom a small solid islet cell tumour was removed at operation, with abolition of symptoms.

Some clinical, biochemical and pathological aspects of this disease are briefly discussed.

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STRICTURE OF THE ŒSOPHAGUS.

By RICHARD FLYNN,

Sydney.

Clinical Record.

F.R.C., a male patient, aged fifty-seven years, consulted me on July 1, 1943, because of difficulty in swallowing which he had experienced continuously during the previous seven years. He stated that when he started to eat his food it went down to behind the lower end of his sternum, where it seemed to block, and he had to vomit it. He had also experienced pain behind the lower end of his sternum since 1941. He had had a severe hæmorrhage in 1934, vomiting half a basinful of blood, and he had had two further severe hæmorrhages in January and July, 1941, but none since the last-mentioned date. At that time he had been examined under the fluoroscope after a barium bolus and the radiographer reported varicose veins of the œsophagus. An ear, nose and throat consultant had also examined his œsophagus with an œsophagoscope, and had found a peculiar mesh of varicose veins about the lower end of his œsophagus. He had lost about six stone in weight since 1936, his weight falling from sixteen stone eight pounds to ten stone three pounds. He had no difficulty in swallowing a glass of water, clear soup or gruel, but if he took solid food it became blocked and he had to vomit it. This suggested that the block was due to a stricture rather than to a true cardiospasm. The patient said that sometimes food also remained in his œsophagus for four or five days. Owing to the long duration of his trouble he was highly introspective, and he handled a long series of radiographs rather like most people do coupons.

I advised him to enter hospital for dilatation of the stricture. This was done on July 5, 1943, by means of a Plummer dilator passed over a previously swallowed silk thread according to the method of Russell. As the metal bougies were passed, it was felt that they traversed an organic stricture rather than that they fell through an achalasia of the œsophagus. A week later bougies up to 45F size were passed by the same method.

The next problem was to identify for certain the nature of the stricture. A test meal examination was made on July 22; this revealed a high curve typical of ulcer—90 units of free hydrochloric acid at one hour and again at one and a half hours. It also revealed the presence of occult blood ("+++" on a basis of "++++" representing pure blood). A provisional diagnosis of peptic ulcer of the œsophagus was made and the patient was referred to Dr. B. P. Anderson Stuart for X-ray examination of his œsophagus and stomach. Dr. Anderson Stuart reported as follows: "There is a constriction of the œsophagus about three or four inches above the stomach. There was only very slight delay in the passage of the meal. A small fleck of barium remained in what appears to be a small ulcer

crater on the posterior wall of the œsophagus at the level of this constriction. There are numerous rather large œsophageal varices in the upper part of the œsophagus and there is slight dilatation of the œsophagus above the constriction."

The patient was advised to follow the customary ulcer *régime*. He reported back on September 10, 1943. His weight had increased to eleven stone six pounds, and he said that he was feeling much better and that he had no pain and no difficulty in swallowing steak. On January 26, 1944, his weight was twelve stone two pounds and he was feeling well.

Comment.

As so frequently happens in medicine, on the evening of the day on which I dilated the patient's œsophagus, I read in the *British Medical Journal* a synopsis of an article by Dick and Hurst in *The Quarterly Journal of Medicine*. In this article they advocated the same treatment as was adopted in this case.

Acknowledgement.

I express my thanks to Dr. A. W. Holmes à Court for allowing me the opportunity of treating this patient.

Reviews.

THE PSYCHOLOGY OF WOMEN.

"MOTHERHOOD" is the title chosen by Dr. Helene Deutsch for the second volume of her projected series of works on the psychology of women.[1] There is a frank admission by the author that a psychoanalytical interpretation is being offered, and this influence is unfortunately responsible for the omission of accepted physiological facts that could be proffered with sounder authority as the underlying reason for her patient's behaviour than those that are offered. The subject matter, however, is far wider than the title suggests and contains many provocative and novel theories.

Dr. Deutsch writes in a most convincing and lucid style and has preserved a satisfying balance in her presentation of actual case histories and deductive observations.

Of particular interest is the section dealing with psychic disorders of pregnancy and the puerperium, and practitioners will do well to accept the author's assertion that toxic and metabolic factors will not completely explain the diverse reactions encountered in these cases. Revolutionary ideas are abundant in her analysis of women's role in active sex life. There is ample evidence of painstaking research, of most extensive contemporary reading, and of an earnest endeavour to make a worthwhile contribution to our limited knowledge on a complex subject. The sequence of the various phases considered is most satisfactory, and the bibliography and adequate index provided round off an excellent work.

REGIONAL ANALGESIA.

H. W. L. MOLESWORTH, an English surgeon, published the first edition of his little book "Regional Analgesia" during the recent great world war. We have now to congratulate him on the success which has brought about the issue of a second edition.[2] In our notice of the first edition, we stated frankly that we could not bring ourselves to join in his approval of paravertebral injections, nor can we do so now, but it is obvious that his own personal experience has been satisfactory, and he trusts his own experience. We can pass beyond the methods that we do not trust, and look with interest at the technique that he has found useful in many operations. It is carefully thought out, it has been tested in practice, and it has succeeded. We recognize, moreover, a sound surgeon, a keen observer and a man of independent mind. He is himself very modest about his work, but notwithstanding his modesty, his experience of local anæsthesia in some important departments of surgery is large and most successful. In England he is something of a pioneer, but he will have converts.

In this second edition he has expanded the range of operations dealt with, and widened technique. He has given more notice to the hæmostatic function of the adrenaline component of the injections than he seemed to do in the first. This we welcome. It is, to us, one of the attractions of this kind of surgery.

There are some errors in the text that are probably due to the typist, and there are two paragraphs dealing with the maxillary nerve (pages 49 and 50) that ought to be reconsidered when a third edition is under preparation.

CLINICAL DEMONSTRATIONS TO NURSES.

HAMILTON BAILEY'S "101 Clinical Demonstrations to Nurses" now appears in its second edition, and consists of a series of plates illustrating various diseases, with a short description of each.[1] The author states in the preface that: "The profession of nursing has become a highly skilled calling, and the modern nurse desires to understand the diseases and injuries of patients under her care." However, to understand the different causes of obstructive jaundice, or to diagnose a cervical adenitis as either Hodgkin's disease or tuberculous adenitis, would not be the desire nor the duty of a nurse. Certainly a final year medical student would need to know these points and those of many other such clinical entities as are described in this little book. The book would in fact be of more value to a medical student than to a nurse, although the phraseology throughout is in simple terms so that the descriptions can be readily appreciated by any nurse. It is surprising in the description of a doubtful lump in the breast to read: "The lump was excised under local anæsthesia and submitted to microscopical examination. It was found to be carcinoma, so she was taken into hospital and a radical operation was performed." One warning that is always timely is given in heavy type: "In the presence of abdominal pain never give a laxative." If that was the only lesson taught it would make the book worth while, provided every nurse heeded it. The illustrations are all of them excellent, many of them being in colour, and, as usual, the printing generally is of the high standard that is expected of the House of Livingstone.

DISORDERS OF THE BLOOD.

THE popularity of "Disorders of the Blood", by Whitby and Britton, is shown by the publication of the fifth edition of the book within eleven years.[2] Extensive revision has brought the text up to date, involving the addition of sixty-two pages, while four new coloured illustrations of the bone marrow have been included.

The term "megaloblast" is limited to Ehrlich's original megaloblast characteristic of the embryo and found in the adult practically only in pernicious anæmia. Its presence indicates abnormal erythropoiesis. Red cells normally differentiate from reticulo-endothelial cells, hæmocytoblasts, through the various stages of proerythroblast, early, intermediate and late normoblasts and reticulocytes to the mature red cells.

In the diagnosis of hæmolytic anæmias, direct evidence of increased blood destruction is shown by hæmoglobinæmia, hæmoglobinuria, methæmalbuminæmia and increased fæcal urobilinogen.

Chapters on the anæmias of infancy and childhood and hæmagglutination and blood transfusion have been extensively revised, and the success in keeping the volume up to date is well illustrated in the detailed but necessarily involved discussion of the increasingly complex Rhesus factors on which so much recent work has been done. The hæmolytic anæmias of infancy are related to the Rh factors, though occasionally ABO incompatibility is responsible.

This volume holds pride of place as the best British textbook on hæmatology.

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[1] "The Psychology of Women: A Psychoanalytic Interpretation", by Helene Deutsch, M.D.; Volume II, Motherhood; 1945. New York: Grune and Stratton. 8¼" x 5", pp. 506. Price: $5.00. Sydney: Angus and Robertson Limited. Price: 37s. 6d.

[2] "Regional Analgesia", by H. W. L. Molesworth, F.R.C.S. (England); Second Edition; 1946. London: H. K. Lewis and Company Limited. 8½" x 5½", pp. 100, with many illustrations. Price: 8s. 6d.

[1] "101 Clinical Demonstrations to Nurses", by Hamilton Bailey, F.R.C.S. (England); Second Edition; 1946. Edinburgh: E. and S. Livingstone Limited. 8¼" x 5¼", pp. 136, with many illustrations, some coloured. Price: 10s. 6d.

[2] "Disorders of the Blood: Diagnosis, Pathology, Treatment and Technique", by Sir Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. (Cantab.), F.R.C.P. (London), D.P.H., and C. J. C. Britton, M.D. (New Zealand), D.P.H.; Fifth Edition; 1946. London: J. and A. Churchill Limited. 9½" x 6", pp. 677, with many illustrations, some coloured. Price: 30s.

The Medical Journal of Australia

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THE PROBLEM OF THE AGED.

THE two groups of persons in the community who should receive more attention than they do are the aged and the insane. The insane are certainly provided for in mental hospitals, but the heads of mental hospital departments complain year in and year out about the intolerable overcrowding to which their charges are subjected, and little if anything is done to remedy matters. The aged are in worse case. Their care is nobody's business, and one can only guess at the enormous extent of the hardship and suffering that are borne by these people with hopeless resignation. The condition of the aged, like that of the insane, has been discussed in these pages on more than one occasion, but no apology need be offered for another reference to it. In actual fact the subject should be mentioned, for these are the days of readjustment after the turmoil of war, the days when men and women from the services are looking for settled homes and peaceful occupations, when industry which had changed its character and multiplied its output to supply the instruments of war must revert to its former spheres of activity and at the same time provide a means of livelihood for its workers. These are the days when man's outlook seems to be entirely new. He has had to face stark reality, he has seen hideous destruction and loss of life without parallel in history, and he knows that hatred is not dead and that fear and distrust are prevalent. It is no wonder that certain values have been lost, nor shall we be surprised when we see that the preservation and service of self occupy the minds of many. This then is the time when the attention of the fit and well should be directed to the plight of those for whom little provision is made in society as it is constituted today.

Before the acutal problem of the aged is discussed, reference must be made to the age distribution of the population. On many previous occasions readers have been reminded that the expectation of life has been greatly increased in the last hundred years as a result of the study and practice of preventive medicine. In a recent paper[1] A. S. Parkes has shown that men over 65 years of age and women over 60 formed 6% of the population of England and Wales in 1901 and 12% in 1941; the percentage of these age groups in 1971 will, he states, be 21. The importance of this observation in any discussion of what is to be done for old people is obvious. Parkes states that the white paper on national insurance contained an estimate that in 1946 there would be 15 pensioners for every 100 contributors, but that in 1970 there would be 32 pensioners for each hundred contributors. Medicine cannot ignore the problem that has arisen. Parkes states quite bluntly that the medical scientist has incurred a grave responsibility in creating vast numbers of old people without at the same time finding out what to do with them. But if medicine has created the problem, it is not solely responsible for the finding of a solution. Medical practitioners, however, as a group see more of the sufferings of old people than are seen by any other group in the community, and they should be in the forefront of any effort that is made to lighten these sufferings.

For purposes of this discussion old people may be divided into two groups—those who retain most of their faculties and are able to enjoy a moderate amount of mental or bodily activity or both, and the more helpless group of those who lead what is really a vegetative existence, whose life is "second childishness and mere oblivion; sans teeth, sans eyes, sans taste, sans everything". In the second group should probably also be placed those old people who are the subject of chronic disease, for they are equally helpless. There is a difference, of course, in the fact that the chronically ill require medical treatment as well as the nursing care that is needed by them and the helplessly senile. When we have the community hospitals for the treatment of the chronically ill, there will be provision for old people in this category, and it will be far better for an old person to be the subject of a chronic disease than to be merely senile. This is a strange commentary to be made in an age in which freedom from disease is looked on as an ideal state. Marjory W. Warren, writing in *The Lancet* of June 8, 1946, on "care of the chronic aged sick", makes a plea for a change of attitude on the part of the medical profession towards the care of those who are afflicted by chronic disease. In the term "chronic aged sick" she includes old people suffering from all the degenerative conditions, from simple uncomplicated senescence to the terminal stages of senile dementia. Though this view nullifies the division of old people into two groups, as already suggested, it is of interest, for Warren thinks that once the medical profession's attitude is changed, the change will be reflected in nursing and other hospital staff personnel. The change of attitude which she demands is a realization of responsibility. This responsibility, she holds, has to do with the retention of the elderly in their own homes where possible. Those who are in a hospital or home should be carefully classified so that their condition may be diagnosed, that they may be adequately treated and properly housed. One of the most important statements made by her is that if a

[1] *The Lancet*, June 22, 1946.

patient has to be admitted to a home the background should be carefully studied. This is not a question of class distinction, but one of mental outlook, that the aged person's lot shall be cast with others who in their earlier days have at least thought about the same things. The subject of so-called rest homes has been discussed on previous occasions, and medical practitioners (and with them all observant lay persons with any touch of humanity in their make-up) know that many of these places are like an open sore on the face of the community. What can be done about the reformation and oversight of these places and the establishment of hostels where they are needed is not at the moment clear. It is one of the subjects to which in these post-war days of readjustment and reconstruction the attention of society should be turned as a matter of urgency. And when this is done some plan should be devised by which husbands and wives who have grown old together and become a charge on the State, should not be separated in their last days.

The problem of the aged who are in possession of all or most of their faculties, remains to be mentioned. The figures quoted by Parkes show that before many years have gone action of some kind will be forced on the community. Parkes states that the only obvious remedial measure is for old folk to work beyond sixty or sixty-five years of age. As things are at present few people can save enough to allow them to retire from work at, say, sixty-five years of age. And the number of persons who on retirement will receive pensions must be relatively small. There is a great deal of remunerative work of different kinds that can be done by elderly people of both sexes. Parkes points out that we have a more rational idea than heretofore of what constitutes the state of being too old to work—we realize that the age at which one becomes too old for a job depends partly on the person and partly on the job. How then can it be discovered when a person is too old for a job and how can he be retrained for a job more suited to his actual mental and physical condition? The former, Parkes reminds us, is primarily a matter of working out standards of necessary performance and is not an easy matter. Many employers and the Medical Research Council of Great Britain, he adds, would like to know the answer. In regard to retraining, Parkes puts the matter well—"it is usually said that only the young can learn easily—you can't teach an old dog new tricks. But it would be much more accurate to say that you can't teach an old dog by the same methods as you teach a young dog." This, he states, is being investigated by experimental and industrial psychologists. There is another side which may be called the preventive side. If it was possible to define certain kinds of work and certain conditions of work suitable for old people, men and women as they grew older might look ahead and prepare themselves for a change of occupation—the old dog would not have so much difficulty in learning new tricks, or at least his learning time would be as long as he chose to make it. Any success in this direction will, of course, depend on the mental and spiritual reserves acquired during the early years of life. In any case, we know that, whether an old person has to earn a living or not, he is a much more pleasant companion or neighbour if he has some constant responsibility within his capabilities than if he is left in idleness with his own thoughts on other people's affairs. Whatever we think of this subject—and there are many other facets to it—individuals and social organizations should make an attempt to understand and deal with its problems. To put the matter on the lowest level, everyone is growing older, and those who can deal with the problems now may some day regret in their own senile unhappiness their present apathy.

Current Comment.

AN ENGLISH REPORT ON MILK.

IN April, 1945, a party of four experts appointed by the Ministry of Agriculture of Great Britain and the Department of Agriculture for Scotland visited the United States of America and Canada to investigate methods of milk production and marketing. The members of the expedition were Mr. J. L. Davies, Milk Production Officer of the Ministry of Agriculture and Assistant General Manager of the Milk Marketing Board (leader), Mr. J. B. Douglas, C.B.E., Vice-Chairman of the Scottish Milk Marketing Board and Chairman of the Kirkcudbright Agricultural Executive Committee, Mr. A. S. Foot, of the National Institute for Research in Dairying, and Mr. L. G. Troup, O.B.E., who was at the time Executive Officer of the Hampshire War Agricultural Executive Committee. The mission concerned itself only with areas primarily devoted to dairy farming; in the United States two weeks were spent in Washington in conference with officials of the Department of Agriculture and in study of the research at the Federal Experimental Farm at Beltsville, and then the States of New York, Wisconsin and Minnesota were visited; in Canada study was confined to the Provinces of Manitoba and Ontario, and the tour finished in Ottawa, in discussions with officials of the Dominion Government Department of Agriculture.

The report of this committee has just been received.[1] It contains an interesting set of recommendations compiled by the committee, which we propose to present shortly. The first is that the Ministry of Agriculture of Great Britain should review cattle-breeding policy in England and Wales, to promote more rapidly the establishment of single-purpose dairy breeds on dairy farms. The committee then suggests that in Great Britain at one large, well-equipped centre long-term cattle-breeding experiments should be undertaken; the work should be done in close association with one of the university agricultural departments. It is thought that the Central Advisory Committee on Artificial Insemination should go into the United States policy of establishing large, cheaply constructed artificial insemination centres opening through local units. Referring to milk recording methods in England and Wales, the committee recommends the following three proposals if any revision of these methods is undertaken: (i) the establishment of a satisfactory recording service for pedigree cattle; (ii) the recording of commercial herds on different and simpler lines; (iii) the inclusion of butter-fat tests in both systems of recording, butter-fat testing to be made compulsory for all pedigree cattle as soon as possible. An active policy of eradicating tuberculosis from milk herds is recommended, by means of the early revival of the Attested Herds Scheme, by eradication on an area basis and by new provisions for the slaughter of all reactors. Special efforts should be made to provide dairy farms with an adequate and cheap electricity supply—an essential for efficient milk production and a help in solving the labour problem. A determined attempt should be made to see that all dairy

[1] "Milk in North America: A Report Submitted to the Ministry of Agriculture and Fisheries and the Department of Agriculture for Scotland by the Members of the Milk Mission following their Investigation in the United States of America and Canada during May and June, 1945"; 1946. London: His Majesty's Stationery Office. 9¼" × 6", pp. 68. Price: 1s. 3d.

farms have a good water supply and that cheap and efficient mechanical cooling equipment is available. Chlorine and other chemicals have been used in the United States for sterilizing milking equipment. The committee is firmly of the opinion that, if quality and marketability in the milk supply are to be promoted, provision should be made for differential payment on butter-fat content as a permanent part of the farmers' milk price mechanism in Great Britain. The milk industry itself should be responsible for testing milk for keeping quality and for providing the necessary farm inspectorate to advise and assist farmers. A system of Ministry licences might be used to provide independent control, if the results of tests were to be the basis of differential milk prices. Referring to fresh cream and ice cream, the committee urges the Ministry to take "early and urgent steps" to obtain legal minimum standards of composition and hygienic quality. The markets should then be developed as soon as sufficient milk is available. More college-trained personnel should be introduced into the milk industry. The committee recommends the establishment in at least one university department of a degree course in dairy technology, including dairy engineering and factory methods of handling and processing milk in factories. Short courses for factory operatives during the winter months should be set up in at least two centres in England and one in Scotland. Research in dairying and ancillary subjects at research institutes should be encouraged and expanded in all possible ways. Finally, the committee recommends investigation on a large scale at one of the research institutes into the development of various crops for feeding dairy cows. The possibility of growing maize for silage and of developing the use of lucerne for hay *et cetera* should receive attention. The management and use of leys should be further investigated. By these means the committee believes that the efficiency of dairy-farming will be improved, because of the better provision of suitable home-produced fodder.

Two points about the dairy herds in America are worthy of mention. Considerable progress has been made, both in the United States and in Canada, in the eradication of tuberculosis from dairy cattle. Apparently tuberculosis-free herds are usual. The testing of animals is undertaken by the Government without charge to the farmer, and the farmer is compensated for tuberculous animals slaughtered up to two-thirds of their commercial value. The second point has to do with the average amount of milk obtained from cows. The average annual yield of cows on dairy farms in the United States and in Canada, where milk production is the main enterprise, is from 700 to 750 gallons per year. This is about 100 gallons higher than the English yield. These results have been obtained by intensive research in animal breeding.

LÖFFLER'S PULMONARY SYNDROME.

THE still increasing use of radiology in the examination of the lungs, both of the sick and of the apparently well, has revealed amongst other things numbers of benign infiltrations of the lungs. Workers in anti-tuberculosis clinics were early impressed with the need for interpreting some of the shadows seen in the pictures obtained from contact children. Perhaps the exponents of "epituberculosis" might have to apply more critical methods today, as it becomes evident that allergic reactions in the pulmonary tissue may occur in response to a number of causes. But it is well to avoid for the present the stimulating paths of controversy and turn to a consideration of the syndrome named after Löffler, who described it in 1932. In his series of 51 patients Löffler described transient infiltrations of the lungs, benign in nature, often migratory, and associated with a local and general eosinophilia. The physical signs were meagre, and the lesions were usually only revealed by radiographic examination. They were believed to be due to a pulmonary response to allergens, but the pathological basis of the changes was obscure. Somewhat similar conditions have been observed in connexion with infestation by animal parasites, but here the changes in the lungs are but part of a well-understood cycle of events. There have been a number of reports also on the autopsy findings in certain cases in which asthmatic attacks had occurred shortly before death, but there was nevertheless a gap which various experimenters have tried to fill by work on animals.

P. A. Herbut and F. R. Kinsey have recently attempted to reproduce the syndrome of Löffler in rabbits.[1] The procedure they adopted was to sensitize rabbits to horse serum by serial injections into the subcutaneous tissue, and after a period of eighteen days to introduce more serum directly into the trachea while the animal was under ether anæsthesia. Some rabbits were given only one intratracheal dose; to others a number of additional doses were given at hourly intervals, and these were repeated the next day. Daily radiographic examinations were carried out, and finally the animals were killed and examined. Pneumonic consolidations were thus produced and their progress was accurately checked. The authors claim that they imitated satisfactorily the syndrome of Löffler in the human subject. Little bodily disturbance was caused, there being no rise in temperature, and the radiological picture was similar. Most of the shadows seen in the lungs were confluent and spread out from the hilar regions, but spotty and nodular shadows were also seen, and as a rule no pleural involvement occurred. The only feature not seen in the films was migration of the shadows. The pathological findings were congestion, œdema, atelectasis and some emphysema, and an eosinophilic infiltration. Hyaline changes, such as have been described in human patients, were found in the epithelium of the bronchi. No eosinophilia was observed in the circulating blood. This work shows that a condition apparently identical with Löffler's syndrome may be produced in animals, in which the findings agree with those postulated and to some extent demonstrated in the human subject. These benign and transient infiltrations of the lung are important. It is known that the so-called virus pneumonia may simulate more serious pulmonary disease, and here is another condition, probably more benign, which may mislead the incautious pessimist.

THE CENTENARY OF ANÆSTHESIA.

ONE hundred years have passed since anæsthesia was adopted for surgical operations. This is made clear in an interesting number of the *British Medical Bulletin* (Number 2, 1946) which is devoted to the centenary of anæsthesia. It was at the Massachusetts General Hospital at Boston that W. T. G. Morton, with the aid of ether anæsthesia, extracted a tooth painlessly on September 30, 1846. The patient inhaled ether from a folded cloth. On October 16, of the same year, Morton convinced many assembled surgeons that surgical anæsthesia could be effectively induced and maintained while removing a tumour from beneath the jaw of a patient who inhaled ether from a valved glass flask containing an ether-soaked sponge. The news soon reached England, and Liston on December 21, 1846, amputated a leg of a patient who inhaled ether from an apparatus devised for the occasion by a chemist named Squire. An interesting review of the development of anæsthesia during recent years by Geoffrey Kaye (Embley Memorial Lecture) was published in this journal last year. This copy of the *British Medical Bulletin* reinforces Kaye's message. It deals with the historical aspect of the subject, but it also reflects the scientific background. The reader is reminded that in other branches of medical practice the outcome of therapeutic procedures is often conjectural and that their choice may be founded more upon pious hope or uncritical faith than on reasoned expectation. The anæsthetist has a task which is precise and unequivocal; the techniques that he employs are designed to effect a known result which is an end in itself. These are facts over which we shall do well to ponder.

[1] *Archives of Pathology*, May, 1946.

Abstracts from Medical Literature.

SURGERY.

The Treatment of Duodenal Ulcer.

W. QUARRY WOOD (*Edinburgh Medical Journal*, December, 1945), in a discussion on the treatment of duodenal ulcer, states that therapy has passed through several phases during the past twenty years. Previously, the pendulum had swung far over to the side of surgery, mainly in the form of gastro-enterostomy. After the unfortunate late complications of this operation became apparent, a reaction followed in favour of medical treatment which has persisted since. It is now widely held that (*a*) the treatment of uncomplicated duodenal ulcer is a medical and not a surgical problem; (*b*) gastro-enterostomy in the absence of well-marked organic stenosis is a bad operation and is universally condemned. In the presence of well-marked organic stenosis gastro-enterostomy is a safe procedure and gives good results; in a case of duodenal ulcer without stenosis when operative treatment is indicated, an extensive partial gastrectomy (subtotal gastrectomy) is the only justifiable procedure. The author discusses alternative operative procedures including gastro-jejunostomy, pyloroplasty, gastro-duodenostomy, partial gastric exclusion, partial fundusectomy, vagotomy and ligature of the gastric blood vessels. Although partial gastrectomy is the most successful procedure for the patient without stenosis, its ultimate effect on the patient is not yet certain. In view of the severity of gastrectomy, the possibility of alternative procedures should still receive consideration.

Treatment of Cancer of the Breast.

ROY F. YOUNG (*Edinburgh Medical Journal*, December, 1945) presents a clinical review of cancer of the breast and antecedent chronic conditions. He bases his views on those patients who have been under his supervision during the past twenty years. It is stated that cancer arises in the breast most commonly during the degenerative period of involution, and the author asks therefore whether there is any probability of finding a line of treatment obviating this as a carcinogenic influence. Carcinogenic factors take a much longer time to be followed by cancer than has been realized, and inquiry into the previous history of a cancer patient, which is a most important matter, must include a considerable period of the patient's life. Chronic trauma to the breast, such as compression or localized pressure, must be avoided. Operation is advisable when chronic cystic disease of the breast is present and local removal is sufficient when a large cyst is present or the condition is limited to a segment of the breast. However, removal of the breast only is probably the wise treatment in cases of widespread cystic disease of the breast. The author states that at the present time the best treatment of cancer of the breast is radical removal followed by irradiation, but that it is rational that a modified form of operation in which the pectoral muscles are left and irradiation is given later, should be given a full trial. Removal should embody all the principles of Sampson Handley's teaching and the fascial planes and the axillary glands should be removed. Hormone treatment which seems to promise much must not be allowed to be announced as a "cure" until it has undergone rigid test by credited clinicians. In advanced cases, irradiation used to destroy the ovarian secretion is worthy of trial.

Operative Closure of the Patent Ductus Arteriosus.

ALFRED BLALOCK (*Surgery, Gynecology and Obstetrics*, February, 1946) discusses the actual operative technique of closure of the patent *ductus arteriosus*. He states that Gross now completely divides and then closes the ductus, because recurrences followed both simple ligation and also ligation by surrounding the ductus with "Cellophane". The author is not satisfied that such a procedure is necessary or safe, and explains the method which he has used in seven cases and now uses. This comprises the use of purse-string sutures at the two extreme ends of the ductus, two through-and-through mattress sutures between the purse-string sutures and a ligature of umbilical tape over the mattress sutures.

Bilateral Petit's Hernia.

F. M. FLICKINGER AND J. C. MASSON (*The American Journal of Surgery*, June, 1946) report a case of bilateral Petit's hernia occurring in a patient who also had an anterior sacral meningocele. The boundaries of Petit's triangle are the iliac crest and the borders of the *latissimus dorsi* and external oblique muscles. In reported cases the height of the triangle has varied up to 7·0 centimetres and the width to 6·0 centimetres. Petit's hernia occurs predominantly on the left side (2·5:1·0) and may be encountered at any age. While the minority have a congenital basis, most of these herniæ are due to trauma or abscess. The trauma may be direct, such as by stab wound, or indirect, as in a fall. A sac is usually present. The symptoms of Petit's hernia are those of hernia elsewhere, that is, the presence of a swelling which may or may not be reducible and may transmit an impulse on coughing. Dyspepsia and constipation are common symptoms and many patients complain of a sense of local pressure or pain. In the differential diagnosis the following must be considered: lipoma, fibroma, cold abscess, hæmatoma and lumbar hernia occurring close to, but not through, Petit's triangle. If the hernia is small and not causing symptoms, conservative treatment is indicated. Fifteen reported cases of repair of a Petit's hernia are discussed. Great care should be exercised in opening the sac, if present, owing to its intimate relationship to bowel and ureter. In one of the reported cases the colon was inadvertently opened. In the case reported by the authors the patient was a woman of forty-one years of age. Bilateral hernia were present, the right being much the larger and containing the right kidney and the greater part of the intestines. There had been attacks of strangulation, but these had been relieved by taxis. Preliminary investigation revealed a pelvic mass which was found to be an anterior sacral meningocele and was removed by the abdominal route. At a later operation the right hernia was explored, and an oval-shaped defect five inches in width was found which was due to congenital absence of the attachment of the *transversus abdominis* and internal oblique muscles to the transverse lumbar processes and the crest of the ilium. The sac was inverted without the peritoneal cavity being opened and the defect was closed by a basket weave repair, seven strips of *fascia lata* being used. Four and a half months later the repair seemed sound and operation for the smaller hernia on the left side was contemplated.

Cauterization of the Pleura in Tuberculous Empyema.

A. BERNOU *et alii* (*La presse médicale*, April 6, 1946) point out that tuberculous empyema, persisting despite lavage and other treatment, reducing the patient's health and so perhaps preventing the completion of a thoracoplasty, may sometimes be successfully treated by cauterization of the pleuropulmonary communications which maintain the empyema. The authors usually use the axillary route, and for purposes of cauterization use the silver nitrite pencil or the galvano-cautery.

Observations on Radical Surgery of the Pancreas.

ALLEN O. WHIPPLE (*Surgery, Gynecology and Obstetrics*, June, 1946) traces the development of radical surgery of the pancreas, and reviews the recent progress in this work. Stressing that the three greatest dangers are hæmorrhage, peritonitis and fistula formation, the author recalls that the earlier surgeons lacked the assistance of vitamin *K* therapy and blood transfusion and did not appreciate the significance of the principles of silk technique. Certain general conclusions have been reached. A one-stage procedure has the advantage of avoiding the massive and vascular adhesions which sometimes form after a first stage, while vitamin *K* therapy eliminates the need for preliminary drainage of the biliary tract to relieve jaundice. The gall-bladder should not be used to reestablish the flow of bile into the alimentary tract, as ascending infection is more likely to occur. It is safer to anastomose the common duct to the jejunum above the site of gastro-jejunostomy. In removing the ampullary area or the head of the pancreas, duodenectomy is necessary because the duodenal blood supply is usually compromised, and (in malignant conditions) to allow adequate radical removal of neighbouring lymphatics and glands. Implantation of the pancreatic duct into the jejunum is advisable and not difficult. Healing is usually satisfactory and doubts regarding interference with fatty digestion have been dispelled. A potential source of difficulty is the uncinate process of the pancreas. This is quite variable embryologically, but may encircle the superior mesenteric vessels or be quite small. When large, it may encircle the superior mesenteric vessels and require very careful removal. The pre-operative care should include measures to discover and treat cardio-vascular, renal and hepatic dysfunctions, and the patient should be

given penicillin, administration commencing twenty-four hours before operation. A stomach tube should be passed and left *in situ* for post-operative suction. Gas-oxygen-ether or continuous spinal anæsthesia has been preferred. The steps of the operation are described briefly, and at the conclusion of the operation (which may occupy three and a half to five hours) a drainage tube is introduced into the subhepatic space, which is kept empty by passing a smaller tube down the lumen, and connecting the latter to a continuous suction apparatus.

The Use of Sulphathiazole in Operation Wounds.

CHARLES H. O'DONNELL, JOSEPH L. PUSCH AND JOHN WINSLAW HIRSCHFIELD (*Surgery, Gynecology and Obstetrics*, March, 1946) found that, in spite of the extensive use of sulphonamides in wounds for the purpose of preventing infection, there was little published evidence to prove that the practice was of value. Many who have claimed that the local use of sulphonamides decreases the incidence of wound infection either have not employed controls or have compared a series in which sulphonamide was used with a control series one or more years previously. Further, they found that there was conflict of opinion in regard to the effect of locally implanted sulphonamides upon wound healing. The authors therefore undertook a study to evaluate the use of sulphonamides locally. Sulphathiazole was used in the form of the powder and also as a 20% suspension in saline solution. Two hundred and seventy clean wounds and 306 contaminated wounds were studied, the drug being used in alternate cases in each of the subdivisions. The authors conclude that sulphathiazole used locally in wounds does not prevent wound infection. There are several reasons for this conclusion. (i) The organisms which cause wound infection are not very susceptible to the sulphonamides. (ii) Dead tissue and foreign bodies, which are of necessity present to some extent in any wound, inhibit the action of sulphonamides. (iii) Sulphathiazole leads to increased bleeding and hæmatoma formation, a factor known to predispose to infection.

Rupture of Malarial Spleen Unassociated with Trauma.

R. R. BEST AND J. F. SCHMID (*Surgery, Gynecology and Obstetrics*, June, 1946) draw attention to the potential rise in traumatic and "spontaneous" rupture of the spleen, owing to the return from overseas of service personnel with splenomegaly. They incline to the belief that so-called spontaneous rupture is probably precipitated by some simple act such as coughing, sneezing or straining at stool, which is forgotten by the patient and not elicited in the history. The enlarged friable malarial spleen is very vulnerable to rupture. Three cases are reported in which rupture of a malarial spleen was unassociated with external trauma. The patients had sudden, mild to severe pain in the left upper quadrant of the abdomen with radiation to epigastrium, loin or left lower quadrant. Nausea and vomiting may occur. Shoulder pain carries great diagnostic weight. Tenderness and rigidity on the left side are significant in any patient with a malarial history. The authors stress the importance of initiating anti-malarial treatment immediately on diagnosis, with the aim of preventing a rigor before or during operation, or in the recovery period. They advise the administration by intramuscular injection of 0·4 gramme of "Atebrin" (half into each buttock), followed by 0·2 gramme every eight hours until the drug can be taken orally, when 0·1 gramme is given thrice daily. One gramme of sodium bicarbonate is given with each dose. Splenectomy is the treatment of choice, and the authors consider that suture and tamponage have no place in the treatment of ruptured malarial spleen.

Early Post-Operative Rising.

JAMES B. BLODGETT AND EDWARD J. BEATTIE (*Surgery, Gynecology and Obstetrics*, April, 1946) have made a critical study of early ambulation after operation. They present a statistical examination of 238 consecutive cases in which early rising was practised and 443 in which it was not. The patients all had major abdominal operations, and only patients who rose from bed either on the first or second post-operative day were considered in the group of early rising. These were compared with patients who remained in bed at least one week after operation. The study occupied three years, and post-operative complications and their causative factors were examined and evaluated. The authors report that the patients who rose early were considerably stronger and had less pain in their wounds. They were able to care for themselves on about the fourth post-operative day and were ready for discharge from hospital much earlier than those in the control group. The incidence of wound disruption and wound infection was reduced in the early rising group. The incidence of pulmonary complications was somewhat lower in the early rising group, but the incidence of deep lung thrombophlebitis was observed to be somewhat greater in the early rising group.

Repair of Large Abdominal Defects by Pedicled Fascial Flaps.

LARGE fascial defects in the upper part of the abdomen as a result of previous operations are difficult of satisfactory closure by any method. Owen H. Wangensteen (*Surgery, Gynecology and Obstetrics*, February, 1946) describes a method of using the ilio-tibial tract of fascia pedicled on the *tensor fasciæ femoris* muscle in the repair of abdominal herniæ. For incisional herniæ with large defects in the upper part of the abdomen, he uses a pedicled fascial flap swung from the lower to the upper part of the abdomen. The defect in the lower part is filled in by the pedicled ilio-tibial tract of fascia.

Primary Resection of Malignant Lesions of the Large Bowel.

WILLIAM B. MCMILLAN (*The American Journal of Surgery*, April, 1946) reports the resection of 27 cases of carcinoma of the large bowel by a one-stage procedure with end-to-end anastomosis and without preliminary caecostomy. The locations of the carcinomata were: hepatic flexure, four cases; transverse colon, six; splenic flexure, five; recto-sigmoid junction, seven; at or just above the level of the perineal reflection, five. There was one death from pulmonary complications. The author stresses the need for thorough pre-operative preparation, the aim being to establish the following criteria: The obstruction is released by suction and a liquid diet is tolerated. The condition of the bowel wall is compatible with safe suturing, that is, the obstruction has been released at least one week. The contents of the bowel have been rendered innocuous by the proper administration of sulphasuxadine over a period of at least four days. The bowel is properly cleansed, a start being made by the use of multiple enemata and castor oil forty-eight hours before operation. Fluid and electrolytic balance have been corrected. A normal blood picture has been obtained by means of blood transfusions and plasma, amino acids, and a diet with a high protein content.

A Device to Simplify End-to-End Bowel Anastomosis.

N. B. STANTON (*The American Journal of Surgery*, June, 1946) presents a method by which end-to-end bowel anastomosis after tumour resection may be simplified by equalizing the diameters of the two segments to be united. Any inequality is due to the fact that the proximal segment is dilated and the distal segment collapsed. The author has found that the lower portion of bowel may be inflated with air until its diameter approximates that of the upper portion. A suitable insufflator connected to a rubber bellows is introduced into the rectum before the patient is draped. The air is introduced after the abdomen has been opened, so that the amount of dilatation is easily observed. A soft clamp is placed on the bowel just distal to the growth to prevent the air from passing into the proximal segment. The method is applicable to the removal of tumours from the transverse, descending or sigmoid colon. No untoward events have attended or followed the use of the method described.

The Management of Aneurysms of the Lower Extremities.

GEORGE D. LILLY (*Annals of Surgery*, April, 1946) reports five cases of aneurysm of the popliteal artery. He points out that such aneurysms are frequent complications of arteriosclerosis, and that, if neglected, they may ultimately create a surgical emergency, because of rupture or thrombosis. In order to avoid this, which frequently terminates in amputation, he advocates careful examination of all patients who complain of peripheral vascular impairment of the lower extremities. If an aneurysm is found to be present, he recommends a lumbar sympathectomy to establish adequate collateral circulation quickly and efficiently and then repair of the aneurysmal defect by performing obliterative endo-aneurysmorrhaphy. The author reviews the recent literature on this subject and concludes that there is ample experimental and clinical evidence to indicate that lumbar sympathetic ganglionectomy will be followed quickly by adequate collateral circulation in a lower extremity. This permits the performance of operation on aneurysms of the lower extremity with comparative safety.

XUM

Bibliography of Scientific and Industrial Reports.[1]

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken from former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 525, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) Those marked with an asterisk may be obtained by approved applicants without cost on making application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

HUTCHENS, JOHN O., *et alii*. A new chamber for the determination of toxicities by total, body or head exposure, to December 12, 1944. (OSRD Report 4585.) Off. Pub. Bd., Report, PB 5908. 1945. 15 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This report describes a dynamic gassing chamber which has certain advantages over standard chambers. The volume is 200 litres—sufficient to permit the exposure of all common laboratory animals with the exception of the goat; and accessories permit not only total, but also head-only and body-only exposures of the various species. The new chamber can be operated at flows as great as five chamber volumes per minute, which is to be compared with 0·5 to 1·0 chamber volumes per minute obtainable in previously described large chambers (EATR 321; OSRD 983). A subsidiary attachment has been fabricated to permit the total, head-only and body-only exposure of mice to gas-containing air flowing at 0·5 to 2·0 miles per hour. The new chamber has been used during the past two years in numerous experiments of the University of Chicago Toxicity Laboratory. Particular attention is directed to the experiments on toxicity of H, Q, L, HNl and HN_3 as a function of flow rate. The design and general appearance of this chamber are apparent from diagrams and photographs. This is a progress report under contract with the University of Chicago.

JACKSON, MARGARET. Röntgenographic technique. (Army Air Forces. Engineering Division ENG-49-698-24.) Off. Pub. Bd., Report, PB 5172. 1944. 20 pp. Price: Microfilm, 50c.; Photostat, $2.00.

An X-ray technique was developed for studying fit of oxygen mask. Exhalation flapper valve action during the face increased the relative contrast between the facial tissue and bones, and between the facial tissue and the oxygn mask. Exhalation flapper valve action during the phases of respiration was studied. Photographs.

KOEPNICK, R. C., AND BENTON, ROBERT S. Head-size standards. (Army Air Forces. Engineering Division. ENG-49-695-32R.) Off. Pub. Bd., Report, PB 5138. 1944. 6 pp. Price: Microfilm, 50c.; Photostat, $1.00.

Sets of head-size standards based upon the dimensions of A.A.F. flying personnel are now available. Appendix 1 gives both the calculated and actual values of the head-size standards. Photographs of head-size standards are attached.

[1] Supplied by the Information Service of the Council for Scientific and Industrial Research.

GAUDLITZ, KARL. *Anaesthetika und Sympathomimetika: Untersuchungen über Derivate des p-oxyphenyläthanolmethylamins (sympatol)*. Off. Pub. Bd., Report, PB 1717. 1942. 59 pp. Price: Photostat, $4.00; Microfilm, $1.00.

This is an inaugural dissertation in German with an English translation, which surveys the research done in the field of anæsthetics. It contains a discussion of a series of compounds that have not yet been published in the literature, the structure of which gives an indication of sympathomimetic and local anæsthetic action. The physical and physico-chemical properties were tested, and these together with the chemical constitution were studied in relation to the pharmacological effects.

HOSKINS, EVERETT L., DIXEY, HERBERT S., AND HALL, CHRISTOFER R. German dental industry. Off. Pub. Bd., Report, PB 1048. 1945. 144 pp. Price: Photostat, $10.00; Microfilm, $1.50.

A detailed survey of the manufacture of important materials, instruments and equipment produced for use by the dental profession. Special attention was given by the investigators to any new or substitute materials discovered, special techniques and manufacturing methods, and present position of German manufacturers with respect to producing for domestic needs. Report includes (1) a summary statement on the industry and on the manufacture of particular products; (2) separate reports on interviews with manufacturers of dental machinery, materials and equipment; and (3) statistics of output, employees, and machinery and equipment of each plant.

JEFFCOTT, GEORGE F. Military and civilian dental education and practice in Germany. Off. Pub. Bd., Report, PB 947. 1945. 15 pp. Price: Photostat, $1.00; Microfilm, 50c.

Dental education, practice and army standing of dentists are described. Military dentistry and maxillo-facial surgery are described in some detail.

RICE, J. B., AND ROSEN, G. Interrogation of General Gerhard Rose, Vice-President of the Robert Koch Institute, Berlin, and Chief Consultant in Tropical Medicine to the German Air Force. Off. Pub. Bd., Report, PB 1101. 1945. 12 pp. Price: Photostat, $1.00; Microfilm, 50c.

Report on information obtained from General Rose on the following diseases: malaria, typhus fever, mite typhus, trichinosis, infectious hepatitis, leptospirosis, bacillary dysentery, amœbic dysentery, cholera, scarlet fever and diphtheria, tularemia, trench fever, relapsing fever, syphilis, gonorrhœa, lymphogranuloma venereum, leishmaniasis, kala-azar, schistosomiasis, filariasis, scabies, rheumatic fever, blood substitutes, sulphonamides. Some information is also given on immunizations in the German Air Force and the use of insecticides and insect repellents.

SCHLUMBERGER, HANS G. The scope of pathology in the German Wehrmacht. Off. Pub. Bd., Report, PB 1102. 1945. 26 pp. Price: Photostat, $2.00; Microfilm, 50c.

Description of the plan of organization for the conduct of pathology in the Wehrmacht and summary of pathological investigations undertaken. Most important of these studies were those on typhus, epidemic hepatitis, acute glomerulonephritis, frost-bite, Wolhynian (trench) fever, bacillary and amœbic dysentery, malaria, diphtheria, tularemia, tuberculosis and coronary occlusion.

UHLE, CHARLES A. W. Medical Department, University of Leipzig. Off. Pub. Bd., Report, PB 964. 1945. 10 pp. Price: Photostat, $1.00; Microfilm, 50c.

Information obtained from interviews with the professors in the various branches of the medical department. Condition of buildings and equipment is described and summary of research and clinical work is given. The following developments are worthy of note: 1. Marfanil was used in the treatment of early gas gangrene with increasingly better results and combining it with gas bacillus serum, amputations in many cases were averted. Marfanil is, chemically, $H_2NO_2S\text{-}C_6H_4\text{-}CH_2NH_2.HCl$. 2. Resistance of the human skin to alternating current was being measured. 3. Experiments were made on the effect of loud tones and overtones in the ear. The Reichswehr was interested in these and in any applications to the modification in equipment. 4. Biological value of synthetic fat.

KEHOE, ROBERT A. Report of investigation of targets concerned with industrial medicine, hygiene and toxicology in German areas occupied by American and British troops. Off. Pub. Bd., Report, PB 1719. 1945. 56 pp. Price: Microfilm, $1.00; Photostat, $4.00.

This report contains information on the nature and incidence of industrial injuries and illnesses. No new method, instruments or principle for the practice of industrial hygiene was formed. A number of specific occupational diseases on which additional information has come to light, such as malignant pulmonary tumours caused by exposure to chromates, tumours of the urinary bladder from exposure to organic amines, and pulmonary neoplasms

among miners caused by exposure to radioactive ores. Toxicology of various fluorine derivatives used as insecticides is presented. Organic chemists at I. G. Farbenindustrie at Elberfeld have investigated insecticidal properties of organic phosphorus compounds. Therapeutic agents such as periston, salicil, *et cetera* are discussed. A drug effect of interest in relation to industrial hygiene is that of dioxystilbœstrol, in the manufacture of which only female workers are employed because of the untoward effects induced in males by the absorption of this material.

PHARMACOLOGY on all compounds tested by I. G. Farben Höchst from April 17, 1935, to December 12, 1939. Off. Pub. Bd., Report, PB 1682. 1935-1939. 796 pp. Price: Microfilm, $8.00; Enlargement Print, $54.00.

Pharmacological report on organic compounds tested by I. G. Farben at Höchst. Compounds nos. 8,000-10,000.

A PICTORIAL report on various aspects of German medical activity. Off. Pub. Bd., Report, PB 2446. 1945. 120 pp. Price: Microfilm, $1.50; Photostat, $8.00.

This report consists of photographs and architects' drawings, accompanied by brief commentaries, on various phases of German medical activity. It deals with such diverse subjects as the use of sponge rubber drain in brain surgery, the rehabilitation of patients with brain injuries, the use of the Küntscher pin in the treatment of fractures, suspension to combat decubitus ulcers, the Kruckenberg plastic operation, rehabilitation of amputees, leg prostheses, and underground hospitals.

RICE, J. B. Tropical medicines and other medical subjects in Germany. Off. Pub. Bd., Report, PB 1718. 1945. 20 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This report covers a wide variety of medical subjects with the emphasis on tropical medicine and communicable diseases. The information was obtained by interviewing a large number of German physicians. The subjects covered are malaria, trench fever, leishmaniasis, dysentery, intestinal coccidiosis, relapsing fever, typhus fever, serum proteins, insect attractants, and antibacterial agents.

SCHADE, H. A. Information on oxygen paradox. Off. Pub. Bd., Report, PB 1384. 1945. 2 pp. Price: Microfilm, 50c.; Photostat, $1.00.

Description of symptoms and effects of a phenomenon affecting those exposed to a mild degree of anoxia. Known as "oxygen paradox", it consists of a hypertoxicity and loss of consciousness immediately following exposure. It is considered important in aviation medicine because (1) it occurs in about 3% of the population; (2) an individual is incapacitated; (3) it follows a type of anoxia which may occur during flight and otherwise not be incapacitating; and (4) incidence in individuals with epilepsy is high.

SCHADE, H. A. Trends in German research work in aviation medicine. Off. Pub. Bd., Report, PB 1382. 1945. 13 pp. Price: Microfilm, 50c.; Photostat, $1.00.

Subjects covered in the order in which they were considered are: high altitude and associated respiratory and circulatory problems; acceleration; problems of nutrition at high altitudes; visual problems. Included in this report are lists of papers and research subjects from three research institutes.

TEUFEL, WILHELM JULIUS, STUTTGART. Four catalogues of the Wilhelm Julius Teufel Company of Stuttgart, manufacturers of prostheses and surgical dressings. Off. Pub. Bd., Report, PB 2449. 1937. 209 pp. Price: Microfilm, $2.50; Photostat, $14.00.

These are four catalogues of the W. J. Teufel Company dealing with orthopædic appliances (parts and instruments for making artificial limbs, orthopædic apparatuses, corsets *et cetera*), bandages and dressings and trusses.

DOCUMENTS and equipment obtained during investigation of German X-ray and associated industries. Booklet (and translation). *"Die Hochfrequenztechnik in der Medizin"*, by Johannes Pätzold, on high-frequency techniques in medicine, including diathermy, electro-surgery, metal foreign body location, and supersonic frequency nerve treatment. Off. Pub. Bd., Report, PB 2176. 1943. 99 pp. Price: Microfilm, $1.00; Photostat, $7.00.

In this treatise an attempt is made, from the point of view of physical and technical theory, to furnish a review of the present-day position in the adaptation of this branch of medicine. The methods in use now are many and varied. There are the direct methods—in which high-frequency currents are conveyed direct to the body of the patient, and the indirect—by which an intermediary comes into use for medicinal purposes. Two newcomers in the indirect field are described—the supersonic wave generator and the Sloan generator for production of hard X-ray radiation. This treatise gives only a limited survey of the physical and electrical problems which the use of high frequencies gives rise to and which limits its applications; physiological and medical points of view are dealt with only in so far as they are necessary for a proper understanding of the subject. Illustrations and a bibliography are found in the 65-page German bulletin. The translation contains 23 pages. The report also contains a bulletin of the *Compagnie Général de Radiologie*, of Paris, entitled *"Camerix; appareil de radiophotographie collective"*.

ZOLLINGER, ROBERT M., *et alii*. Medical, dental and veterinary education and practice in Germany as reflected by the Universities of Leipzig, Jena, Halle and Erlangen. Off. Pub. Bd., Report, PB 1786. 1945. 55 pp. Price: Microfilm, $1.00; Photostat, $4.00.

The heads of the medical departments of the above schools were interviewed. The physical condition of the schools, bed capacity of the clinics, enrolment, training and medical research are discussed. The principles of therapy in medicine on the following subjects are considered: sulphonamide therapy, care of wounds, burns, wound infections (gas gangrene, tetanus), neurosurgery, chest surgery, abdominal surgery and vascular surgery, anæsthesia, vitamins, malnutrition, communicable disease. Medical education was curtailed 50% and the calibre of students is inferior. Sulphonamide therapy was widely used; penicillin was unknown. Dental education, oral health and prevention of dental caries are discussed. Veterinary education, food control and other subjects of medical interest are dealt with.

BARBER, H. J. Dutch Scientific Institutions in Utrecht and Amsterdam. Off. Pub. Bd., Report, PB 2042. 1945. 17 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This report consists of interviews with four Dutch scientists—Professor Koningsberger, Professor Jansen, Dr. Timmerman and Professor Kögl. These Dutch scientists have been able to continue with some of their scientific work under considerable difficulty. Professor Koningsberger's work has no immediate bearing on penicillin production. It is stated, however, that the main product from the growth of *Penicillium expansum* which Koningsberger has worked on is almost certainly Patulin. The Dutch workers have called it Expansin. Kögl claims to have substantiated his observations (subsequently disputed by other workers) that d-glutamic acid and not the normally occurring isomer is produced in malignant tissue. This is produced by a different mechanism from that which synthesizes the l-isomer. Kögl has shown that his (β) biotin differs slightly from the (a) biotin of du Vigneaud.

BEAVER, WILLIAM C. German medical kit for airplanes. (Army Air Forces. Engineering Division. ENG-49-698-25.) Off. Pub. Bd., Report, PB 2961. 1944. 12 pp. Price: Microfilm, 50c.; Photostat, $1.00.

A description of a captured German medical kit for airplanes. Consists of a compactly arranged set of emergency medical supplies, including splints, tourniquet, bandages, surgical instruments, first-aid supplies, and an aluminium case containing syringe, hypodermic needles and injection materials. Aluminium wire splints are bent so as to form sides and ends of the container, surrounded by an oiled paper covering. A canvas outside covering is also provided. Appendix has photographs and detailed description of contents.

DOCUMENTS and equipment obtained during investigation of German X-ray and associated industries. Siemens' electromedical sales bulletins, including electro-surgical equipment, diathermy equipment, "galvanic" equipment, ultra-violet lamps and "infro-red" lamps. Off. Pub. Bd., Report, PB 2180. No date. 49 pp. Price: Microfilm, $1.00; Photostat, $6.00.

Titles of these sales bulletins of Siemens-Reiniger-Werke of Berlin include: *Elektromedizinische Apparate für die allgemeine ärztliche Praxis*; *Kurzwellen in der Zahnheilkunde*; *Pantostaten, die Apparate für alle Zwecke der Elektrodiagnostik und Elektrotherapie*; *Für Kurzwellentherapie*: *Ultratherm*; *Siemens-Apparate für Elektrochirurgie*; *Siemens-Dental-Diathermieapparate zum Wurzelbehandeln, Blutstillen, Zahnbleichen und zum Schneiden und Durchwärmen mittels Hochfrequenzstroms.*

DOCUMENTS and equipment obtained during investigation of German X-ray and associated industries. Siemens' "Konvulsator" (electric shock therapy unit); technical articles regarding equipment and techniques, instructions manual, and wiring diagrams. Off. Pub. Bd., Report, PB 2178. No date. 30 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This report consists of four pamphlets and a diagram. Their titles are: 1. *Das Gerät zur Elektrokrampferzeugung und seine physikalischen Grundlagen (Auszug aus einem am 25. VI. 1940, in der Physikalisch-Medizinischen Sozietät der Universität Erlangen gehaltenen Vortrag)*, by Johannes Pätzold; 9 pages. 2. *Die Electrokrampftherapie*, by Hermann Olbrich, including a bibliography; 4 pages. 3. *Gebrauchs-Anleitung zum Siemens-Konvulsator*; *Gerät zur Elektrokrampf-Behandlung*; 11 pages. 4. *Simens Konvulsator, Das Gerät zur Elektrokrampf-Behandlung der Psychosen*, including a bibliography; 5 pages.

XUM

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held on July 11, 1945, at the Children's Hospital, Carlton, DR. ROBERT SOUTHBY, the Acting President, in the chair. Parts of this report appeared in the issues of July 6 and July 20, 1946.

Toxoplasmic Encephalomyelitis.

DR. E. GRAEME ROBERTSON read a paper entitled "Toxoplasmic Encephalomyelitis" (see page 449), and showed two patients suffering from the condition.

DR. L. WAIT congratulated Dr. Robertson on the diagnosis of a difficult case. He said that he had read about toxoplasmosis in a cursory way and had not connected the second patient shown with the condition. The child had been sent to Dr. Wait from the Women's Hospital with a diagnosis of hydrocephalus; but he was impressed by the microphthalmos, and Dr. Nancy Lewis had observed chorioretinitis. The X-ray findings in the skull were reported as within normal limits, and the Wassermann test produced no reaction. A subsequent X-ray examination, however, did reveal obvious intracranial calcification, and a more careful review of the first X-ray film revealed its presence even then. It could easily be mistaken for an artefact. Dr. Wait said that he would be on the look-out for such cases, and credit must be given to Dr. Robertson for drawing attention to the syndrome.

DR. W. W. MCLAREN congratulated Dr. Robertson on the new knowledge disseminated by his paper. He asked whether all children afflicted with the disease had microphthalmos. He also asked what was the relative incidence of microcephalus and hydrocephalus.

DR. GUY SPRINGTHORPE said that he had studied Sabin's article; it was complete. Dr. Springthorpe had wondered who would be the first to discover the first case in Australia, and he thought it fitting that the honour had fallen to Dr. Robertson. Dr. Springthorpe asked whether the condition had been seen in Australian animals, and whether it would be possible to establish methods of investigation in Australia. He had noted with interest that in the acute form of the disease in children and in the pulmonary form in adults, both sulphapyridine and sulphadiazine in ordinary doses had been found of therapeutic value.

DR. ROBERT SOUTHBY said that he had seen patients with a condition resembling this entity, especially those with one small eye and a certain degree of hydrocephalus, as well as many patients with hydrocephalus which had become arrested soon after birth.

Dr. Robertson, in reply, said that the condition was much more common than was realized. Probably all degrees of severity existed and many minor affections had not been described. Dr. Southby was not able to give statistics of patients with microphthalmos and hydrocephalus. He had spoken to Professor F. M. Burnet concerning diagnostic laboratory methods. At present the opportunity of obtaining material for animal inoculation was being awaited. The tests were rather complicated and the complement fixation test was not yet adequate. Dr. Robertson said that he would appreciate contact with patients likely to die of this disease, so that material could be sumbitted for examination. Toxoplasma had been obtained from the cerebro-spinal fluid of a child, but this was unusual. As far as he knew, the condition had not been met with in Australia.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

COURSE IN BACTERIOLOGY.

THE Melbourne Permanent Post-Graduate Committee announces that it has arranged a course in bacteriology suitable for candidates for the following diplomas and degrees: M.R.A.C.P.; D.G.O., Part II; D.L.O., Part II; D.O., Part II; M.D., Part II; M.S., Part II. The course will be conducted by Professor Rubbo at the lecture theatre, Women's Hospital, Carlton, commencing on Monday, October 7, 1946, at 4.30 o'clock p.m., and continuing on each Monday at the same time until November 25.

Following this there will be three lecture demonstrations suitable for M.R.C.O.G. and D.G.O., Part II, candidates.

Early in 1947, a similar small special series of lectures will be provided for D.L.O., Part II, and D.O., Part II, candidates.

LECTURES IN MELBOURNE.

THE Melbourne Permanent Post-Graduate Committee announces that a series of lectures designed for candidates for the M.D., Part II, and M.R.A.C.P. examinations will commence on October 8, 1946, and will be conducted from 4.30 to 5.30 o'clock p.m. each Tuesday and Thursday till early in December. Details of the syllabus will be published at a later date. The fee for this course is eight guineas.

Applications from those proposing to attend should be forwarded to the Post-Graduate Committee's office, College of Surgeons, Spring Street, C.1., as soon as possible. Those entitled to financial assistance under the Commonwealth Rehabilitation Training Scheme, part-time, are requested to indicate this fact on their application.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

WEEK-END COURSE AT NEWCASTLE.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end course will be held at Newcastle on Saturday and Sunday, October 26 and 27, 1946, in conjunction with the Central Northern Medical Association.

The programme for the course will be as follows:

Saturday, October 26, 1946.

At the Nurses' Lecture Room, Newcastle Hospital.

2 p.m.: Registration.
2.30 p.m.: "Injuries to the Knee Joint", Dr. R. V. Graham.
4 p.m.: "Medical Aspects of Thyreotoxicosis", Dr. A. W. Morrow.

Sunday, October 27, 1946.

At the Nurses' Lecture Room, Newcastle Hospital,

10 a.m.: "Recent Advances in the Treatment of Sterility", Professor Bruce T. Mayes.
11.30 a.m.: "Injuries to the Wrist and Foot", Dr. R. V. Graham.
2 p.m.: "Recent Therapeutic Advances in Medicine", Dr. A. W. Morrow.
3 p.m.: "Can We Make Breech Presentation Easier and Safer?", Professor Bruce T. Mayes.

The fee for the course will be £1 1s., except for members of the defence forces, who may attend the course without fee. Those intending to be present are requested to notify Dr. E. J. Egan, Honorary Secretary, Central Northern Medical Association, 69, Hunter Street, Newcastle, as soon as possible.

Special Correspondence.

CANADA LETTER.

FROM OUR SPECIAL CORRESPONDENT.

THE outstanding health news of the past months has been the nation-wide epidemic of poliomyelitis. In Montreal alone it is probable that the number of cases will reach 1,000 before the end of the season. Cases have been reported from Ontario and as far west as the Rocky Mountains. However, the west coast Province of British Columbia has had but three cases, all before June of this year. Maritime Provinces will scarcely exceed one dozen cases. Most markedly affected have been the boys and girls' camps in the

Laurentian Mountains and in parts of Ontario. In one of these camps it would appear that the centre of infection was one tent, as the overall camp hygiene facilities were excellent thanks to DDT. On an Indian reservation where sewage is known to have polluted a river, the source of infection might have been considered intestinal. In one camp most of the cases were characteristized by limb paralysis. In another, however, most of the cases were bulbar in type. Naturally a great interest has been shown in curare and other drugs reputed to have helped in other epidemics. Effects of this drug and others are being studied intensively by Dr. Herbert Jasper, of the Montreal Neurological Institute, with one of the excellent electromyograms which he developed for the Canadian Army during the war. In addition, studies are being made with the electro-encephalograph of non-paralytic, paralytic and encephalitic cases in children. There has been an intensive campaign to sell the so-called jacket or cuirasse-type of respirators which can be operated from 6-volt storage batteries either in ambulance or in aircraft. They have proven their usefulness on many occasions recently.

The Province of Saskatchewan is again leading the way in the transport of patients and has recently purchased another Norseman air ambulance. During the summer, the plane, operating in the northern section of the Province, has been equipped with pontoons for landing on the numerous lakes in that area. A flat charge of $25 per call has been made for the service, but in needy cases no charge is made.

As part of the new movement in Canada for better nutrition a cookbook for British brides has just been issued through the Wartime Information Board for the use of British brides of Canadian servicemen returning home. The very practical matter of feeding their new husbands with Canadian food has been simply stated in this excellent booklet. It is reminiscent of the Air Force stations in Canada which had to bow to the Australian craving for steak and eggs!

The Montreal Neurological Society will commence its autumn programme on October 9 when Dr. A. McGhee Harvey, the recently appointed Professor of Medicine at Johns Hopkins Medical School, will speak on the "Biochemistry of Neuromuscular Diseases". He will be followed a week later by Commander Livingstone, recently returned from the United States Navy, on "The Physiological Effects of High Velocity Missile Wounding". It is expected that Sir Henry Dale will give the Hughlings Jackson Memorial Lecture during the month of October.

The list of appointments to university positions of doctors returning from the services is daily becoming more impressive. The former head of Medical Research for the Royal Canadian Air Force, Group Captain G. E. Hall, A.F.C., has been made Dean of Medicine of the University of Western Ontario, at London, Ontario, and has been designated as the next President of that University to take office next year. Dr. Donald McEachern has returned to McGill University as chief of the Neurological Service of the Montreal Neurological Institute, and as Neurologist-in-Chief to the Royal Victoria Hospital of Montreal. Wing Commander Alfred Elliott, formerly overseas consultant in ophthalmology of the Royal Canadian Air Force, has been made Professor of Ophthalmology at the University of Toronto and Ophthalmologist-in-Chief to the Toronto General Hospital.

Obituary.

ARTHUR WALDO CONNELLY.

WE are indebted to Dr. A. E. Rowden White for the following appreciation of the late Dr. Arthur Waldo Connelly:

The recent death of Dr. Arthur Waldo Connelly at his home in Burke Road, Upper Hawthorn, Victoria, is a great loss to the community, as he was a well-known and popular suburban medical practitioner. Connelly was born on March 10, 1870, in Bendigo, his father being Thomas James Connelly, who founded the first hardware store in that city. It is interesting to note that the store is still in existence, having passed from the family into the hands of a company. Young Connelly was educated at the Bendigo Grammar School and later graduated from the University of Melbourne in 1894. Afterwards he spent a year in India and on his return was elected to the staff of the Bendigo Hospital. During the height of the gold activity in Western Australia, he went to Kalgoorlie in 1898 and was taken into partnership by Dr. O'Meahan and later entered private practice at Boulder City and was appointed a surgeon to the Kalgoorlie Government Hospital. He lived at Boulder for twenty-three years, excepting for a period of two years when he served with the Australian Infantry Forces abroad in the 1914-1918 war, most of the time being spent at Number 2 Australian General Hospital, Wimeureux, France. He came to Melbourne in 1921 and was in active suburban practice for twenty-five years, right up to the time of his death. The members of the staff of Number 2 Australian General Hospital, in France, will recall happy memories of his pleasant geniality and staunch friendship while they were awaiting the great German "push" in 1917-1918 and of the anxious times when the enemy broke through in March, 1918.

We offer our sincere sympathy to his widow and three married daughters.

JOHN CLARK MUIR.

WE are indebted to Dr. A. E. Rowden White for the following appreciation of the late Dr. John Clark Muir:

On August 7, 1946, at Kidderminster, England, the sudden death of Dr. John Clark Muir terminated a picturesque career of the life of a Melbourne graduate so well-known to crowds of young medical graduates from the whole of Australasia who visited England during the past two generations for post-graduate work. Muir was born in Queensland and was educated at Scotch College, Melbourne, and graduated at the University of Melbourne towards the end of last century. After spending two years in residence at the Women's Hospital, Melbourne, he went to London, Edinburgh and Baltimore to further his post-graduate studies and qualify himself as a gynæcologist. In London he went into residence at 4, Endsleigh Gardens, which was an unofficial Australasian Club, and for years it was the Mecca of most students and graduates from Australia and New Zealand. Muir became so imbued with the life of London that he continued to reside at 4, Endsleigh Gardens for many years and to enjoy the companionship of fresh batches of young graduates from overseas. His name became a tradition among the men who, having completed their studies and returned home, recommended all their young friends who proposed visiting London to "look up" Jack Muir for advice as to the best way of expediting their studies in Great Britain, Vienna or the United States of America. Muir qualified F.R.C.P. and F.R.C.S. Edinburgh, and then decided to reside permanently in London, which he did for many years, at Grey's Inn and afterwards at Gowers Street until the German "blitz" destroyed his flat and compelled him to retreat to Kidderminster. Muir was a most friendly and lovable soul and always a popular person throughout his school and University days. He was considered an authority on the Charles Dickens London, and many a happy and instructive hour he has given overseas visitors in jaunts to various spots in the world's capital, made famous by the great writer. It is for this and many other admirable qualities that Jack Muir's name will always be revered by so many Australians.

Naval, Military and Air Force.

DECORATIONS.

COLONEL ALFRED PLOMLEY DERHAM has been created a Commander of the Military Division of The Most Excellent Order of the British Empire, for gallant and distinguished services in Malaya, in 1942.

Colonel E. R. White, Lieutenant-Colonel A. E. Coates, O.B.E., Lieutenant-Colonel E. M. Sheppard and Major B. H. Anderson have been mentioned in dispatches for gallant and distinguished services in Malaya in 1942.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Downie, David Alfred William, provisional registration, 1946 (Univ. Sydney), Wallsend District Hospital, Wallsend.

Richardson, Stephen, provisional registration, 1946 (Univ. Sydney), Balmain and District Hospital, Balmain.

Australian Medical Board Proceedings.

TASMANIA.

THE undermentioned have been registered pursuant to the provisions of the *Medical Act*, 1918, of Tasmania, as duly qualified medical practitioners:

Hayes, Ross Abbott, M.B., B.S., 1945 (Univ. Melbourne), Malvern, Victoria.

Rank, Benjamin Keith, M.B., B.S., 1934 (Univ. Melbourne), M.S., 1937 (Univ. Melbourne), F.R.C.S., (England), 1938, F.R.A.C.S., 1942, Royal Hobart Hospital, Hobart.

Travers, Lennard Gilmour, M.B., B.S., 1930 (Univ. Melbourne), F.R.C.S. (Edinburgh), 1935, Royal Hobart Hospital, Hobart.

THE FEDERAL MEDICAL WAR RELIEF FUND.

THE following contributions to the Federal Medical War Relief Fund have been received:

Queensland.

D. B. Walker, £10 10s.
W. A. Mackay, E. J. Reye, £10.
W. H. Nette, £8 8s.
I. G. Hooper, £5 5s.
E. Reimers, £5.
D. F. Millar, £3 3s.
J. I. Hains, K. Hossack, £2 2s.
H. C. Fox, £1.
Total: £57 10s.
Grand total: £14,879 3s. 6d.

Books Received.

"Anatomical Eponyms: Being a Bibliographical Dictionary of those Anatomists whose Names have become Incorporated into Anatomical Nomenclature, with Definitions of the Structures to which their Names have been Attached and References to the Works in which They are Described", by Jessie Dobson, B.A., M.Sc., with a Foreword by F. Wood Jones; 1946. London: Baillière, Tindall and Cox. 8¼" × 6¾", pp. 250. Price: 30s. net.

"An Introduction to Biochemistry", by W. R. Fearon, M.A., Sc.D., M.B.; Third Edition; 1946. London: William Heinemann Medical Books Limited. 8¾" × 5½", pp. 580, with illustrations. Price: 21s. net.

"Sternal Puncture: A Method of Clinical and Cytological Investigation", by A. Piney, M.D., M.R.C.P., and J. L. Hamilton-Paterson, M.D., M.R.C.S., with a foreword by the Right Honourable Lord Horder, M.D., F.R.C.P.; Third Edition; 1946. London: William Heinemann Medical Books Limited. 8¼" × 5½", pp. 96, with many illustrations, some of which are in colour. Price: 15s. net.

"Ophthalmology in the War Years", edited by Meyer Wiener, M.D.; Volume I (1940-1943); 1946. Chicago: The Year Book Publishers Inc. 9¼" × 6¾", pp. 1176.

"Infant Feeding", by V. L. Collins, M.D. (Melbourne), M.R.C.P. (London), D.C.H. (London); Fourth Edition; 1946. Melbourne: W. Ramsay (Surgical) Pty. Ltd. 8¾" × 5¾", pp. 74. Price: 4s. 3d.

Medical Appointments.

Dr. S. G. Stevens has been appointed Deputy Medical Superintendent, Mental Hospitals Division, Department of Public Health of New South Wales.

Dr. R. M. Windeyer has been appointed Government Medical Officer at Manilla, New South Wales.

Dr. D. N. Kekwick has been appointed Medical Officer of Health, Mosman Park Road Board, Western Australia.

Dr. W. Gilfillan, Dr. A. J. Hakendorf and Dr. F. G. T. Turner have been appointed honorary clinical assistants to the Dermatological Section, Royal Adelaide Hospital, Adelaide.

Diary for the Month.

OCT. 1.—New South Wales Branch, B.M.A.: Council Quarterly.
OCT. 2.—Western Australian Branch, B.M.A.: Council Meeting.
OCT. 2.—Victorian Branch, B.M.A.: Branch Meeting.
OCT. 3.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 4.—Queensland Branch, B.M.A.: Branch Meeting.
OCT. 4.—New South Wales Branch, B.M.A.: Annual Meeting of Delegates.
OCT. 8.—Tasmanian Branch, B.M.A.: Ordinary Meeting.
OCT. 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
OCT. 8.—New South Wales Branch, B.M.A.: Organization and Science Committee.
OCT. 11.—Queensland Branch, B.M.A.: Council Meeting.
OCT. 15.—New South Wales Branch, B.M.A.: Medical Politics Committee.
OCT. 16.—Western Australian Branch, B.M.A.: General Meeting.
OCT. 17.—Victorian Branch, B.M.A.: Executive Meeting.
OCT. 17.—South Australian Branch, B.M.A.: Council Meeting.
OCT. 22.—New South Wales Branch, B.M.A.: Ethics Committee.
OCT. 23.—Victorian Branch, B.M.A. Council Meeting.
OCT. 24.—New South Wales Branch, B.M.A.: Clinical Meeting.
OCT. 25.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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